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Development of an evidence base for the study of dynamic palatal dysfunction in horses

Development of an evidence base for the study of dynamic palatal dysfunction in horses

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Abstract

Palatal dysfunction is the most common form of dynamic upper respiratory tract (URT) obstruction affecting racehorses and therefore is of great importance to the horseracing industry. There is an urgent need to develop a robust evidence base in this area of equine sports medicine. The aim of this thesis was to establish the evidence base for the diagnosis, aetiopathogenesis and treatment of dynamic palatal dysfunction and to undertake targeted studies to address key areas.

There was poor experimental evidence to fully explain the aetiopathogenesis, which impacted on the efficacy of treatments available. A systematic review of intervention studies showed that decision making for choice of intervention is currently based on inadequate published data, personal experience or anecdote rather than on evidence based data. Many studies were based upon horses without a definitive diagnosis of this condition and there was poor understanding of appropriate outcome metrics for intervention studies.

A novel technique of overground endoscopy was shown to produce diagnostic images of the URT in exercising horses. A comparison of overground endoscopy and treadmill endoscopy showed that dorsal displacement of the soft palate (DDSP) was diagnosed significantly less often during overground endoscopy. A study of overground exercise tests showed that DDSP was more likely to be diagnosed when longer test distances were performed. Certain endoscopic characteristics of the soft palate epiglottis were shown to be associated with progression of palatal instability to DDSP. The effect of palatal dysfunction on measures of ventilation gas exchange were evaluated. One form of palatal instability was shown to be detrimental to gas exchange, although this was not as great as the detrimental effect of DDSP.

The value of using race performance as an outcome measure was assessed. Several factors were identified which show that outcome measures such as earnings may not be ideal for assessing intervention efficacy.

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Finally I am indebted to the trainers and horses involved in these studies.

Author's Declaration

I declare that the work in this dissertation was carried out in accordance with the requirements of the University's Regulations and Code of Practice for Research Degree Programmes and that it has not been submitted for any other academic award. Except where indicated by specific reference in the text, the work is the candidate's own work. Work done in collaboration with, or with the assistance of, others, is indicated as such. Any views expressed in the dissertation are those of the author.

Kate Allen ....

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Glossary

ACC	Arytenoid cartilage collapse
ADAF	Axial deviation of the aryepiglottic folds
CAPSO	Cautery assisted palatal stiffening operation
CO_2	Carbon dioxide
CPAP	Continuous positive airway pressure
DDSP	Dorsal displacement of the soft palate
EBM	Evidence based medicine
EIPH	Exercise induced pulmonary haemorrhage
EMG	Electromyography
F	Breathing frequency
$FetCO_2$	End-tidal carbon dioxide concentration
$FetO_2$	End-tidal oxygen concentration
FN	False negative
FP	False positive
HE	Hyoepiglotticus muscle
HSTE	High-speed treadmill examination
HTP	Hyoidthyroidpexia
IS	Injection Snoreplasty

LED	Light emitting diode
LHS	Laryngohyoid support device
LR	Likelihood ratio
LTF	Laryngeal tie-forward
LVP	Levator veli palatini
MCID	Minimal clinically important difference
MyHC	Myosin heavy chain
NAD	No abnormality detected
Nd:YAG	Neodymium-doped yttrium aluminium garnet
NH	National Hunt
NPV	Negative predictive value
O_2	Oxygen
OG	Overground
OPS	Oropalatal seal
OSA	Obstructive sleep apnea
Perf.I.	Performance Index
PI	Palatal instability
PPV	Positive predictive value
PWC	Pharyngeal wall collapse

RE	Race earnings
RLN	Recurrent laryngeal neuropathy
RPR	Racing Post rating
S	Staphylectomy
SB	Standardbred
s.d.	Standard deviation
SM	Sternothyroid myectomy
SPC	Soft palate cautery
ST	Sternothyroideus tenectomy
STPD	Standard temperature and pressure dry
TB	Thoroughbred
TF	Timeform rating
TM	Treadmill
TN	True negative
TP	True positive
TS	Topspeed rating
TT	Tongue tie
TVP	Tensor veli palatini
UK	United Kingdom

UPPP	Uvulopalatopharyngoplasty
URT	Upper respiratory tract
US	United States
VCC	Vocal cord collapse
$\dot{V}CO_2$	Carbon dioxide production
$\dot{V}_E$	Minute ventilation
$\dot{V}O_2$	Oxygen consumption
$\dot{V}O_{2max}$	Maximal oxygen consumption
V_T	Tidal volume
WB	Warmblood

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Part 1

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Chapter 1 General Introduction

Evidence based medicine (EBM) is considered increasingly important in human medicine and over the last decade there has been a gradual trend towards the development of evidence based veterinary medicine. The degree to which evidence based practice is performed in human specialties varies across disciplines. Evidence based sports medicine and athletic training is only recently emerging. If equine sports medicine is also to be seen as a viable and valid specialty then there must be an evidence base behind it. It is imperative for the future of equestrian disciplines that the health, training and welfare of horses used in sport is as highly regarded as the health and training received by human athletes.

There are numerous definitions and descriptions of evidence based medicine, but the most widely quoted definition is *'the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients'* (Sackett *et al.* 1996). Sackett *et al.* (2000) went on to describe the concept of evidence based medicine as the *'integration of best research evidence with clinical expertise and patient values'*. Others have defined evidence based medicine as *'the use of mathematical estimates of the risk of benefit and harm, derived from high-quality research on population samples, to inform clinical decision making in the diagnosis, investigation or management of individual patients'* (Greenhalgh 2010). Therefore the defining feature of evidence based medicine is *'the use of figures derived from research on populations to inform decisions about individuals'* (Greenhalgh 2010).

Sackett *et al.* (2000) summarized five essential steps in practicing evidence based medicine:

1. To convert information needs into answerable questions
2. To track down efficiently the best evidence with which to answer these questions
3. To appraise the evidence critically
4. To implement the results in our clinical practice
5. To evaluate our performance

In this thesis an evidence based approach will be used to study dynamic palatal dysfunction in the horse. Palatal dysfunction is a form of dynamic upper respiratory tract (URT) obstruction and comprises dorsal displacement of the soft palate (DDSP) and palatal instability (PI) (Lane *et al.* 2006a). Dorsal displacement of the soft palate occurs when the caudal border of the soft palate becomes displaced to a position above the epiglottis resulting in obstruction of the rima glottidis (figure 1.1) (Parente *et al.* 2002; Franklin *et al.* 2004; Lane *et al.* 2006a).

1.1 Dorsal displacement of the soft palate

Palatal instability has been described as progressive dorso-ventral billowing movements of the caudal portion of the soft palate, with flattening of the ventral surface of the epiglottis against the dorsal surface of the soft palate (figure 1.2) (Kannegieter and Dore 1995; Ahern 1999a; Tan *et al.* 2005; Lane *et al.* 2006a). Palatal instability may or may not progress to DDSP during exercise (Lane *et al.* 2006a). Some authors have suggested that PI always pre-exists DDSP and therefore believe it to be a manifestation of the same condition (Lane *et al.* 2006a), whereas others have suggested that DDSP may occur in the absence of PI (Barakzai and Hawkes 2010). A syndrome of severe billowing of the rostral aspect of the soft palate in ponies has been described (Allen *et al.* 2007); however this condition appears to be less common and shows some differences to palatal instability of the caudal soft palate as described above.

1.2 Palatal instability

Palatal dysfunction is the most common form of dynamic URT obstruction affecting racehorses referred for investigation of abnormal respiratory noise and/ or poor performance (Morris and Seeherman 1991; Kannegieter and Dore 1995; Martin *et al.* 2000; Parente *et al.* 2002; Tan *et al.* 2005; Lane *et al.* 2006a). However, the prevalence of this condition in the general thoroughbred racehorse population is unclear. A trainer survey performed in the UK suggested a prevalence of DDSP of approximately 6.5% (Franklin 2002). However, the findings of a more recent UK yard survey suggest that the true value might be considerably higher, as 13 of 67 (19%) of randomly selected horses from a single training yard were observed to have DDSP during exercise (Pollock *et al.* 2009).

In general, URT obstructions in horses are thought to affect athletic performance by increasing the resistance to airflow, leading to either a reduction in airflow or an increase in pressures required to maintain that airflow (Rehder *et al.* 1995; Franklin *et al.* 2002a; Weishaupt 2005). A reduction in airflow reduces alveolar ventilation which subsequently affects arterial oxygenation (Bayly *et al.* 1984; Durando *et al.* 2002; Boyle *et al.* 2006) and oxygen uptake (Franklin *et al.* 2002a). An increase in airway resistance results in increased work of breathing which would lead to premature diaphragmatic fatigue or to competition for oxygen and cardiac output between respiratory and locomotor muscles. In man it has been suggested that respiratory muscle fatigue may subsequently affect exercise tolerance through a reduction in ventilation, an alteration in breathing mechanics or an increased sensation of dyspnoea (Romer and Polkey 2008). However it was also considered likely that a respiratory muscle fatigue-induced metaboreflex would limit exercise tolerance. It was proposed that diaphragmatic fatigue during exercise leads to a sympathetically mediated vasoconstriction of limb locomotor muscle vasculature, thus exacerbating peripheral fatigue and intensifying effort perceptions (Romer and Polkey 2008). This mechanism has not yet been studied in the exercising horse.

Naturally occurring DDSP has been shown to affect ventilation, airflow, airway pressures and gas exchange during exercise (Rehder *et al.* 1995; Franklin *et al.* 2002a). Minute ventilation decreased by approximately 13%, primarily through a reduction in tidal volume, and maximal oxygen consumption decreased by 10% (Franklin *et al.* 2002a). Peak expiratory flows were significantly decreased, but there were no significant alterations in inspiratory flows (Franklin *et al.* 2002a). During periods of DDSP pharyngeal and tracheal inspiratory pressures became less negative, pharyngeal expiratory pressures became less positive and tracheal expiratory pressures became more positive (Rehder *et al.* 1995). Experimentally induced DDSP was also confirmed to increase expiratory impedance; however there were some differences in the observations compared with naturally occurring DDSP (Holcombe *et al.* 1998). Experimentally induced rostral PI was shown to have no significant effect on expiratory pharyngeal or tracheal pressures. However tracheal inspiratory pressures were significantly more negative and there was a trend for pharyngeal inspiratory pressures to be less negative, although this only approached statistical significance (Holcombe *et al.* 1997a). When horses with naturally occurring PI were compared to a group of normal horses and a group of DDSP horses (prior to displacement) no significant differences in ventilation or gas exchange were identified (Franklin 2002).

Due to the dynamic and intermittent nature of DDSP, obtaining a definitive diagnosis is often considered to be challenging. Furthermore the aetiopathogenesis of the condition is incompletely understood and as a result numerous treatment options have been described. However, the efficacy of treatments remains controversial and there is little consensus about how best to treat this condition.

Consequently dynamic palatal dysfunction is of great importance to the horseracing industry and there is an urgent need to develop a robust evidence base in this important area of equine sports medicine. The result will be great gains in equine welfare and performance. The most important reason for practicing evidence based equine medicine is to improve the quality of care of horses through the identification and promotion of practices that work and the elimination of practices that are either ineffective or harmful. Firstly it was necessary to establish what the evidence base was and where new research was needed. The aim of this project was to establish the current evidence base for the diagnosis, aetiopathogenesis and treatment of dynamic palatal dysfunction, with particular focus on the thoroughbred racehorse. The degree to which evidence based medicine could be practiced was discussed. Following this, ways to begin developing the evidence base were suggested. Furthermore specific studies were undertaken with the aim of improving the evidence base. The layout of this thesis is divided into two main sections. Chapters in the first section review the evidence base and chapters in the second section consist of specific research studies undertaken to address key areas.

Chapter 2 A critical review of the diagnostic methods for dynamic palatal dysfunction

2.1 *Introduction*

The aim of this chapter was to critically review the literature on the diagnostic methods for dynamic palatal dysfunction. In a practical sense a diagnostic test is useful only when the result influences the management of that patient. As the treatment options for palatal dysfunction are different to those for other dynamic URT obstructions, obtaining a definitive diagnosis is important. There are welfare implications to horses undergoing inappropriate surgeries, in addition to the lack of performance improvement that would be obtained.

To determine the suitability of a diagnostic test, specific studies need to be undertaken which report the diagnostic accuracy. Guyatt *et al.* (2006) described four main characteristics of a valid diagnostic study:

1. The study assembles an appropriate spectrum of patients
2. The study applies the diagnostic test and the reference standard to all patients
3. The results are interpreted each blind to the other
4. The study repeats itself in a second, independent ("test") set of patients

Due to the lack of scientifically rigorous data, all reported diagnostic approaches to dynamic palatal dysfunction have been described in this chapter. The evidence to support or refute these approaches has been critically analysed. The diagnostic approaches used in textbooks and publications were described. Electronic databases (including MEDLINE, PUBMED, ISI Web of Science, CAB abstracts, EMBASE and IVIS) were searched for review articles and for studies investigating diagnostic accuracy. Bibliographies of referenced textbooks and the reference lists of all retrieved studies were also hand-searched for further relevant studies. Where possible the data was extracted from the primary studies and calculations of specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV) and likelihood ratios (LR) were made (Petrie and Sabin 2005). Forest plots were generated to graphically present the interaction between specificity and sensitivity[1].

Sensitivity and specificity are used to assess the reliability of a diagnostic test (Petrie and Sabin 2005). Sensitivity is the proportion of individuals with the disease who are correctly identified by the test. Specificity is the proportion of individuals without the disease who are correctly identified by the test. Predictive values provide information about how likely it is that the individual has or does not have the disease, given its test result (Petrie and Sabin 2005). The PPV is the proportion of individuals with a positive test result who have the disease and the NPV is the proportion of individuals with a negative result who do not have the disease. The sensitivity and specificity provides information about the test in general, where as the predictive value informs what a particular test result means for the patient in front of you (Greenhalgh 2010). Likelihood ratios can be calculated to assess how useful a test is (Petrie and Sabin 2005). The LR for a positive result is the ratio of the chance of a positive result if the patient has the disease to the chance of a positive result if the patient does not have the disease. Accuracy is the proportion of all tests which have given the correct result (Greenhalgh 2010). The higher a test's sensitivity, specificity, PPV and NPV (closer to 1) the more accurate that test is. The larger the LR of a positive test and the farther the LR of a negative test is from 1 (the smaller it is), the more accurate that test is (Guyatt *et al.* 2006)

Where possible each diagnostic criterion will be assessed against treadmill endoscopy which has routinely been considered to be the 'gold standard' (Barakzai 2007a; Desmaizieres *et al.* 2009). The potential limitations of considering treadmill endoscopy as the reference standard or gold standard will be discussed later. Although this thesis is focused primarily on the thoroughbred racehorse, studies assessing standardbred racehorses and sport/ pleasure horses have also been included in this chapter, due to the low number of publications.

2.2 Presenting complaint

Typically racehorses with dynamic palatal dysfunction are referred for investigation of poor athletic performance and/ or abnormal respiratory noise. However, numerous other forms of URT obstructions exist which also present with poor performance and/ or abnormal respiratory noise (Franklin 2008). Furthermore, there are also many non-URT causes of poor athletic performance (Morris and Seeherman 1991; Martin *et al.* 2000). Not surprisingly, horses referred for abnormal respiratory noise are more likely to have an URT abnormality than those referred only for poor performance (Tan *et al.* 2005).

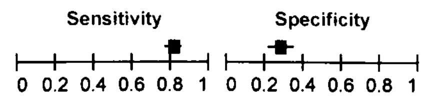
Racehorses with DDSP, in addition to a general history of poor racing performance, may have a more specific history of 'fading towards the end of a race' or 'stopping abruptly toward the end of a race' (Cook 1965; Heffron and Baker 1979). It is probable that the sudden onset of DDSP during racing, leading to a dramatic reduction in ventilation (Franklin *et al.* 2002a) may cause an abrupt decrease in pace. With the exception of paroxysmal atrial fibrillation (and acute orthopaedic injuries which are likely to be apparent at the end of the race) few other conditions occur with such a sudden onset during racing. Most other dynamic URT obstructions are gradually progressive during the exercise period. Therefore it is likely that fatigue at the end of a race in normal horses and horses with compromised athletic performance and premature fatigue due to other disorders may also appear to 'fade towards the end of the race'.

2.3 Abnormal respiratory noise

A clinical and experimental study showed that characteristically during episodes of DDSP a 'gurgling' expiratory noise is generated by vibration of the free border of the soft palate (Franklin *et al.* 2004). A clinical study which measured sound frequencies showed that PI was associated with increased noise in the inspiratory spectra (Franklin 2002).

Five studies reported the proportion of horses with a history of abnormal respiratory noise which were subsequently confirmed to have DDSP during treadmill endoscopy and one study of horses confirmed to have PI. It appears that all of these publications were retrospective studies performed on hospital case records. The publication by Lane *et al.* (2006b) was based entirely on thoroughbred racehorses, and the publications by Parente *et al.* (2002) and Tan *et al.* (2005) included a large proportion of thoroughbred racehorses. A history of abnormal respiratory noise was reported in 75% of horses with PI (Lane *et al.* 2006b) and 58% (Tan *et al.* 2005), 62% (Parente *et al.* 2002), 71% (Lumsden *et al.* 1995), 81% (Martin *et al.* 2000) and 85% (Lane *et al.* 2006b) of horses with DDSP. Only one study reported this information within a larger population of racehorses with a broad spectrum of competing conditions, therefore sensitivity and specificity can only be calculated for this study (Lane *et al.* 2006b) (figure 2.1, table 2.1). The results show that the sensitivity is fairly high, in that most horses with this condition have a history of abnormal noise, however the specificity is very low and reflects the fact that most other URT obstructions also cause abnormal noise.

Study	TP	FP	FN	TN	Sensitivity	Specificity
Lane et al. 2006	317	151	73	59	0.81 [0.77, 0.85]	0.28 [0.22, 0.35]



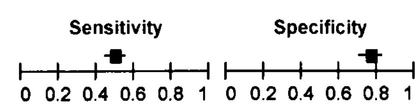
2.1 Forest plot showing the diagnostic accuracy of trainer reported history of abnormal noise in thoroughbred racehorses diagnosed with palatal dysfunction during treadmill endoscopy

Table 2.1 Shows the diagnostic features of abnormal respiratory noise detected by the trainer as the diagnostic test compared to palatal dysfunction during treadmill endoscopy as the gold standard

Study	Sensitivity	Specificity	PPV	NPV	Accuracy	LR for a positive result	LR for a negative result
Lane *et al.* 2006b	0.81	0.28	0.68	0.45	0.63	1.13	0.68

It is also possible to assess the diagnostic accuracy of a history of ‘gurgling’ from this study (figure 2.2, table 2.2). Fifty seven percent of horses confirmed with DDSP had a history of ‘gurgling’ noise and 38% of horses with PI had a history of ‘gurgling’ noise (Lane *et al.* 2006b). This suggests that a proportion of horses diagnosed as having PI during treadmill endoscopy might in fact be experiencing DDSP during training or racing that was not recreated during the treadmill exercise test.

Study	TP	FP	FN	TN	Sensitivity	Specificity
Lane et al 2006	195	49	195	161	0.50 [0.45, 0.55]	0.77 [0.70, 0.82]



2.2 Forest plot showing diagnostic accuracy of a trainer reported history of 'gurgling' noise in Thoroughbred racehorses confirmed to have palatal dysfunction during treadmill endoscopy

Table 2.2 Shows the diagnostic features of gurgling noise detected by the trainer as the diagnostic test compared to palatal dysfunction during treadmill endoscopy as the gold standard

Study	Sensitivity	Specificity	PPV	NPV	Accuracy	LR for a positive result	LR for a negative result
Lane *et al.* 2006b	0.50	0.77	0.83	0.45	0.59	2.17	0.65

These results show that a trainer history of 'gurgling' noise is more specific for palatal dysfunction than a more general history of abnormal noise. The higher PPV indicates a greater proportion of horses with a history of gurgling noise have DDSP during exercise than those with the more general history of abnormal noise. This result is not surprising to clinicians and textbooks had already previously stated that '*The noise ... associated with DDSP ... is somewhat specific in that it occurs during expiration and has a snoring character, quite different from the inspiratory noises associated with other dynamic inspiratory airway abnormalities*' (Holcombe and Ducharme 2004). Epiglottic entrapment is the only other URT condition also reported to cause a vibrant expiratory noise (Barakzai 2007b). The accuracy of the specificity and sensitivity calculations in figures 2.1 and 2.2 may be affected by the fact that 25% of DDSP cases and 45% of PI cases were diagnosed with additional forms of URT collapse (Lane *et al.* 2006a). It is probable that the additional forms of URT collapse also caused abnormal respiratory noise and that this noise might have been detected by the trainer instead of/ as well as the noise from the palatal dysfunction.

On the basis of the early studies the existence of 'silent displacers' i.e. that DDSP occurred during exercise but did not result in generation of abnormal respiratory noise was proposed (Lumsden *et al.* 1995; Ahern 1999a; Martin *et al.* 2000; Parente *et al.* 2002). However, as these studies were based on the trainer reporting the noise, it was unclear whether some horses with DDSP do not make any abnormal noise or whether some trainers had failed to detect the abnormal noise. Extracting data from the study by Lane *et al.* (2006b) it was possible to study this further (table 2.3).

Table 2.3 Shows the proportion of horses with palatal dysfunction in which abnormal noise was detected by trainer and veterinary surgeon

Diagnosis during treadmill endoscopy	Trainer reported history of abnormal noise	Abnormal noise detected by veterinary surgeon
Palatal dysfunction (PI & DDSP) n=390	81%	82%
DDSP n=237	85%	89%
PI n=152	75%	72%

The results suggest there is little difference in the detection of abnormal noise by trainer or by veterinary surgeon. However this study did suggest that the 89% of DDSP horses detected to have abnormal noise by the veterinary surgeon were all described as characteristic rough expiratory sounds. This would suggest that the veterinary surgeon is able to recognise 'gurgling' in a substantially higher proportion than the 57% of DDSP horses in which gurgling was detected by the trainer.

It is probable that detection of abnormal noise was considerably easier for the veterinary surgeons in this study, utilising sound recordings made at the horse's nostrils, in comparison to detection of the noise in the field or race by the trainer/ jockey, where external influences such as wind noise and other horses can be influential. Although these results confirm that some horses do not appear to make abnormal respiratory noise despite the presence of DDSP, it appears that this is likely to be closer to 10% of horses rather than the 30% that had been suggested in earlier studies. This suggests that the ability of the jockey/ trainer in identifying abnormal noise and recognising 'gurgling' may be important or that the presence of abnormal noise may be intermittent in nature. It is also likely that the proportion of silent displacers in these studies may not represent the total population, as it is probable that many horses that make a characteristic abnormal noise undergo surgery without a treadmill examination having been performed.

The noise associated with PI is quieter than the noises associated with DDSP and other forms of URT collapse (Franklin 2002) and hence may not always be detected by the jockey, trainer or veterinary surgeon.

2.4 Spectral analysis

It has been shown that sound can readily be recorded during ridden exercise in an arena and during ridden exercise on the gallops (Attenburrow 1978; Burn *et al.* 2006; Derksen 2007).

Expiratory spectral analysis frequency peaks in the 20-90 Hz range have been observed during DDSP (Derksen *et al.* 2001; Franklin *et al.* 2004). The low frequency peak in some horses may not be easily distinguished by the human ear, explaining why some horses have no audible sound detected. In addition, horses had additional high frequency inspiratory noise during DDSP. In contrast, the expiratory spectra of horses with PI did not differ from normal horses (Franklin

2002). However there was increased inspiratory noise in both the low frequency (~500Hz) and higher frequency (~1.5KHz) range. Initial research therefore suggested that spectral analysis had potential as a diagnostic technique.

However, recent research (J.F. Burn and S.H. Franklin, unpublished data) suggests that spectral analysis is unlikely to be an accurate method of establishing a diagnosis for other forms of URT collapse apart from DDSP. Most upper airway disorders in which an abnormal inspiratory noise is heard produce sound frequencies in the same spectrum as each other. In addition the same sound frequencies are observed in normal horses, albeit at lower intensities. Therefore, it has been suggested that the nasopharynx is acting as a resonant chamber.

2.5 Abnormal breaths and swallows

Horses with palatal dysfunction may be presented with a history of mouth breathing, breath holding, gulping or swallowing during exercise. Franklin (2002) found that horses with palatal dysfunction exhibited significantly more abnormal breaths (swallows and prolonged respiratory cycles) than normal horses. Subsequently Pigott *et al.* (2010) have also shown an increased frequency of swallowing prior to DDSP compared with normal horses.

It has also been shown that horses with experimentally induced DDSP may alter their breathing pattern to a 2:1 locomotor respiratory ratio (Holcombe *et al.* 1998). However, it is unclear what proportion of horses with naturally occurring palatal dysfunction alter their breathing pattern and to what extent this may occur with other forms of URT obstruction (Weishaupt *et al.* 1998).

Mouth breathing during exhalation is recognised by fluttering of the cheeks as air is diverted underneath the soft palate, through the mouth, and is suggested to be a specific sign that a horse has displaced its soft palate (Holcombe and Ducharme 2004).

2.6 Ultrasound

Laryngeal ultrasound was first described by Chalmers *et al.* (2006). A subsequent study by the same group was undertaken to investigate whether ultrasound assessment of laryngohyoid position was predictive of DDSP (Chalmers *et al.* 2009). The study was performed in 56 racehorses (19SB, 37TB), of which 26 were confirmed with DDSP during treadmill endoscopy. A significant relationship was found between the depth of the basihyoid bone at rest and the occurrence of dorsal displacement of the soft palate at exercise, whereby on average a more ventral location of the basihyoid bone is present in horses with dorsal displacement of the soft palate. The difference between DDSP and non-DDSP groups was less than 2mm (table 2.4). Other measures of laryngohyoid position were not found to be associated with dorsal displacement of the soft palate. No significant differences between TB and SB were identified.

Table 2.4 Shows the mean (+s.d) of the depth of the basihyoid bone at the base of the lingual process for the DDSP group and the non-DDSP group

	Depth of basihyoid bone at base of lingual process (cm) mean (s.d.)	
DDSP	1.18 (0.2)	P<0.03
No DDSP	1.34 (0.26)	

Potential problems with this measurement are that although a neutral head position was described, this was not standardised between horses. A recent radiographic study showed that head position was certainly influential to the laryngohyoid relationship (McCluskie *et al.* 2008), although the dorsoventral hyoid movement was not assessed. Furthermore, as this is a transcutaneous measurement, the distance is likely to be readily influenced by the pressure on the ultrasound probe. However, for this study intraobserver repeatability was high for this measurement.

In a subsequent study performed at a different centre, 148 horses underwent treadmill endoscopy and laryngeal ultrasound. Seventy five horses were subsequently confirmed to have DDSP. The author reported that no characteristic ultrasound findings could be identified in the DDSP group. Although the figures were not included the author also reported that no significant differences in the depth of the basihyoid were found between the DDSP and the non-DDSP group (Garrett 2010).

2.7 Resting endoscopy

Endoscopy of the upper airways whilst the horse is at rest is a widely available diagnostic test. During the resting endoscopic examination it has been suggested that intermittent DDSP, soft palate ulceration and a small or flaccid epiglottis might be indicative of DDSP during exercise. It has also been suggested that during resting endoscopy the most important signs indicative of

DDSP are the ease with which DDSP is induced, the duration of displacement and how readily the horse is able to correct it by swallowing (Lumsden *et al.* 1995; Holcombe and Ducharme 2004), however these factors have not been appropriately studied. Nasal occlusion may aid assessment of nasopharyngeal function. It has previously been shown that during a 60 second nasal occlusion the upper airway pressures generated are equivalent to those observed during exercise (Holcombe *et al.* 1996). The respiratory stimulant lobeline has also been used in practice to simulate airflows during the endoscopic assessment of nasopharyngeal function (Marlin *et al.* 2000). However in one study lobeline induced hyperventilation did not simulate the flow rates needed to induce collapse of unsupported tissue of the nasopharynx and larynx (Weishaupt *et al.* 1998).

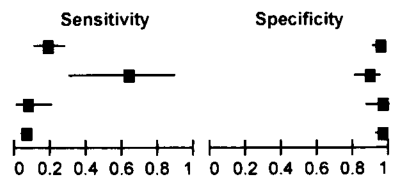
Although some clinicians consider DDSP during the resting examination when the endoscope is withdrawn from the trachea sufficient criteria to establish a diagnosis (Parente and Martin 1995; Woodie *et al.* 2005a), many clinicians do not consider this abnormal (Lumsden *et al.* 1995; Holcombe and Ducharme 2004; Barakzai and Dixon 2011). Certainly Parente and Martin (1995) showed that 52/76 horses displaced the soft palate following tracheal endoscopy, however only 23/76 displaced the soft palate during exercise.

The prevalence of DDSP during resting endoscopy varies widely between studies, and probably reflects different populations studied and differences in endoscopy protocol. Six studies provided some information which can be used to draw comparisons of resting and exercising palatal dysfunction. All studies were retrospective analysis of hospital records. The percentage of DDSP confirmed cases that displace the soft palate at some point during the resting endoscopic examination was 8% (Lane *et al.* 2006b), 20% (Kannegieter and Dore 1995), 26% (Barakzai and Dixon 2011) and 51% (Parente *et al.* 2002). Of the horses confirmed by treadmill endoscopy to have dynamic palatal dysfunction, 7% (Lane *et al.* 2006b), 8% (Franklin *et al.* 2006) and 19% (Barakzai and Dixon 2011) experienced DDSP at rest. The study by Davidson *et al.* (2011) was unusual in that a greater proportion of horses (17%) experienced DDSP at rest, compared with only 5% of horses which experienced DDSP during exercise or 11% which experienced palatal dysfunction during exercise.

The study by Parente *et al.* (2002) was based only on DDSP horses with no equivalent data for comparison horses, therefore five studies provide sufficient data to calculate diagnostic accuracy.

However, two of these studies were based entirely on sport horses (Franklin *et al.* 2006; Davidson *et al.* 2011). There was some variation in the reported results as to whether resting findings were compared to a diagnosis of DDSP during exercise or palatal dysfunction during exercise. Where possible both were calculated from the data provided (figures 2.3 and 2.4). These studies show that the specificity of DDSP during resting endoscopy is high, however the sensitivity is generally low.

Study	TP	FP	FN	TN	Sensitivity	Specificity
Barakzai and Dixon 2011	18	9	78	176	0.19 [0.12, 0.28]	0.95 [0.91, 0.98]
Davidson et al 2011	7	10	4	82	0.64 [0.31, 0.89]	0.89 [0.81, 0.95]
Franklin et al 2006	3	2	36	52	0.08 [0.02, 0.21]	0.96 [0.87, 1.00]
Lane et al 2006	26	8	364	202	0.07 [0.04, 0.10]	0.96 [0.93, 0.98]

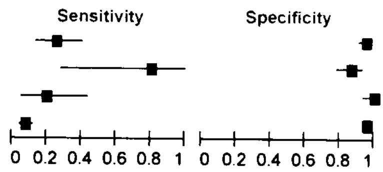


2.3 Forest plot showing diagnostic accuracy of DDSP during resting endoscopic examination for palatal dysfunction during exercise

Table 2.5 Shows the diagnostic features of DDSP during resting endoscopy as the diagnostic test compared to palatal dysfunction during treadmill exercise as the gold standard

Study	Sensitivity	Specificity	PPV	NPV	Accuracy	LR for a positive result	LR for a negative result
Barakzai and Dixon 2011	0.19	0.95	0.67	0.69	0.69	3.8	0.85
Davidson *et al.* 2011	0.64	0.89	0.41	0.95	0.86	5.82	0.40
Franklin *et al.* 2006	0.08	0.96	0.6	0.59	0.59	2	0.96
Lane *et al.* 2006b	0.07	0.96	0.76	0.36	0.38	1.75	0.97

Study	TP	FP	FN	TN	Sensitivity	Specificity
Barakzai and Dixon 2011	12	9	35	176	0.26 [0.14, 0.40]	0.95 [0.91, 0.98]
Davidson et al 2011	4	13	1	85	0.80 [0.28, 0.99]	0.87 [0.78, 0.93]
Kannegeiter and Dore 1995	4	0	16	55	0.20 [0.06, 0.44]	1.00 [0.94, 1.00]
Lane et al 2006	19	15	218	348	0.08 [0.05, 0.12]	0.96 [0.93, 0.98]



2.4 Forest plot showing diagnostic accuracy of DDSP during resting endoscopic examination for DDSP during exercise

Table 2.6 Shows the diagnostic features of DDSP during resting endoscopy as the diagnostic test compared with DDSP during treadmill exercise as the gold standard

Study	Sensitivity	Specificity	PPV	NPV	Accuracy	LR for a positive result	LR for a negative result
Barakzai and Dixon 2011	0.26	0.95	0.57	0.85	0.81	5.2	0.78
Davidson *et al.* 2011	0.80	0.87	0.24	0.99	0.86	6.15	0.23
Kannegeiter and Dore 2006	0.20	1.0	1.0	0.77	0.79	-	0.8
Lane *et al.* 2006b	0.08	0.96	0.56	0.61	0.61	2	0.96

Epiglottic abnormalities and soft palate ulceration were described less often. Six percent (Lane *et al.* 2006b), 14% (Parente *et al.* 2002) and 20% (Kannegieter and Dore 1995) of DDSP confirmed horses had epiglottic abnormalities on resting endoscopic examination. Only 5-10% (Kannegieter and Dore 1995; Parente *et al.* 2002) of horses with confirmed DDSP on a treadmill had evidence of soft palate ulceration. In addition Hobo *et al.* (1995) reported that of 117 horses with DDSP during resting endoscopy, only 5 (4.3%) had ulceration of the free border of the soft palate.

Ninety two percent of horses with palatal instability had a normal resting endoscopic examination (Lane *et al.* 2006b). In addition, the three horses with palatal billowing described by Kannegieter and Dore (1995) all had normal resting endoscopic examination.

In contrast to the resting laryngeal function grading systems the repeatability of resting findings for palatal dysfunction have not been studied.

2.8 History and resting endoscopy together

Only one study analysed the use of history and resting endoscopy together (Lane *et al.* 2006b). In combination a history of gurgling and the presence of palatal or epiglottic abnormalities at rest showed a significant association with palatal dysfunction during exercise. However, the final model which included both factors, was still considered a poor predictor of palatal malfunction. When resting endoscopy and reported noises were taken together there was still a 35% misdiagnosis rate (Lane *et al.* 2006b).

2.9 Post-exercise (resting) endoscopy

Endoscopy post-exercise has been reported as a diagnostic method in some centres (Woodie *et al.* 2005a; Marcoux *et al.* 2008), however most horses with DDSP correct the displacement at the end of exercise, therefore post exercise endoscopy is generally considered to be of little value (Llewellyn and Petrowitz 1997; Morris and Seeherman 1990; Morris and Seeherman 1991). In contrast there are apparently normal horses that displace when first pulling up after exercise (Parente and Derksen 2006). Changes to the breathing strategy occur as the horse slows from maximal exercise and appear to be accompanied by relaxation of the pharyngeal musculature (Parente and Derksen 2006). At the cessation of maximal exercise, the horse is experiencing hypoxic and hypercapnic physiological drive. High tidal flow rates with limited tidal volumes during intense exercise are replaced with high tidal volumes and progressively decreasing flow rates in recovery (Curtis *et al.* 2006). Therefore, it has been suggested that any conclusion based on an endoscopic examination after exercise, particularly with respect to the functional stability of the pharynx, may be inaccurate (Parente and Derksen 2006).

2.10 High-speed treadmill endoscopy

Many of these studies suggest that dynamic palatal dysfunction cannot be accurately diagnosed from the presenting history or during a resting endoscopic examination. Therefore, high-speed treadmill endoscopic examination has become an invaluable tool in the assessment of the URT during exercise (Morris and Seeherman 1990; Kannegieter and Dore 1995; Martin *et al.* 2000; Tan *et al.* 2005; Lane *et al.* 2006a) and is frequently considered the 'gold standard' method.

Unfortunately the cost, time implications and misconceptions regarding the safety (Franklin *et al.* 2010) of the technique mean that this is not always performed and many horses still receive a diagnosis on the basis of history of abnormal noise and resting endoscopic findings (Franklin 2002).

However, there is the potential for misdiagnosis with the use of high-speed treadmill endoscopy also. It is well known that treadmill exercise does not replicate exercise in the field. There are significant differences in heart rate, blood lactate, stride frequency and stride length between field exercise and treadmill exercise (Barrey *et al.* 1993a and b; Sloet van Oldruitenborgh-Oosterbaan and Barneveld 1995; Courouce *et al.* 1999; Sloet van Oldruitenborgh-Oosterbaan and Clayton 1999; Courouce *et al.* 2000; Evans 2004). Exercise on an uninclined treadmill is less strenuous for the horse resulting in lower heart rates and blood lactates (Courcouce *et al.* 1999). Stride lengths are longer and stride frequencies lower during treadmill exercise than field exercise (Barrey *et al.* 1993; Courouce *et al.* 1999). It is not clear to what degree respiratory variables would differ, as a direct comparison of respiratory parameters between treadmill and field exercise has not been possible. For normal Thoroughbreds at gallop respiratory frequency and stride frequency will be the same. Furthermore, tidal volume is associated with stride length. This would suggest that during treadmill exercise, horses might have lower breathing frequency and higher tidal volumes than during field exercise. As tidal volume and respiratory time both increase it is unclear whether this affects upper airway pressures. As a result of these differences and the fact that race conditions are not truly replicated, it is assumed that false negative results may occur during treadmill endoscopy (Lumsden *et al.* 1995).

It remains unclear when horses were referred for gurgling noise but DDSP was not observed during treadmill endoscopy whether the inaccuracy is truly in the trainer's history or whether in fact it might be in the treadmill examination. As a result of this some clinicians use treadmill endoscopy as a means to eliminate alternative sources of dynamic upper respiratory tract obstruction before making a diagnosis of DDSP by exclusion (Parente *et al.* 2002; Lane *et al.* 2006a).

Another limitation of treadmill endoscopy for diagnosis of dynamic palatal dysfunction is that repeatability has not been appropriately studied. Certainly it is unclear whether horses displace their palates on every occasion and at the same point of the exercise test. Only one study could be

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Another limitation of treadmill endoscopy for diagnosis of dynamic palatal dysfunction is that repeatability has not been appropriately studied. Certainly it is unclear whether horses displace their palates on every occasion and at the same point of the exercise test. Only one study could be identified in which one horse was confirmed to have DDSP during high-speed treadmill exercise on three occasions (Peloso *et al.* 1992).

It would seem likely that inter-observer agreement for DDSP should be high, as it is an all or nothing event. However there does appear to be some slight variation between studies. Some studies would note that the presence of DDSP whatever the duration constituted a diagnosis, whereas some centres suggest that DDSP must be present for 8 seconds to constitute a diagnosis (Rehder *et al.* 1995). There is also variation between studies as to whether DDSP on pulling up was considered a diagnosis. It is likely that the agreement between observers for PI is not as high. It appears from these studies that some authors do not recognise PI as a diagnosis.

2.10.1 Exercise test

It has been suggested that accurate conclusions from an endoscopic examination on a high speed treadmill cannot be drawn without specifying the exertional effort (Parente and Derksen 2006). DDSP commonly occurs during the period of maximum exercise intensity when fatigue of pharyngeal muscles is likely to occur (Lumsden *et al.* 1995). Therefore it is important that the exercising conditions should simulate the horse's normal working conditions as closely as possible. It was suggested that the horse should be in condition and prepared for the treadmill examination as if it were the date of a race (Parente and Derksen 2006).

Design of exercise tests is difficult as it is currently not fully understood how the parameters of the exercise test not only affect work effort and oxygen consumption but also airflows, upper airway pressures and work of breathing. It has previously been reported that the effect of gradient on oxygen uptake is substantial (Eaton 1994) and that the effect of increasing gradient on the cost of transport is greater than the effect of increases in speed (Schroter and Marlin 2002). Inclined exercise is used in testing to increase work effort without increasing speed, thereby reducing the risk of musculoskeletal injury (Evans 1994). However, inspiratory pressures become more negative at higher speeds (Ducharme *et al.* 1994), and it is unclear whether horses tested at slower speeds on an incline experience the same inspiratory pressures that occur when exercising at faster speeds during a race.

DDSP is an intermittent condition, therefore if all the same conditions (e.g. speed, head/neck flexion, fatigue) are not reproduced a false negative outcome may be obtained. Thus the test employed is extremely important in obtaining an accurate diagnosis (Parente 1998). Several studies confirm the importance of continuing exercise to the point of fatigue in order to establish a diagnosis (Stick *et al.* 1990, Kastner *et al.* 1998). Other studies have reported that DDSP may occur during the exercise test at changes in exercise intensity (Peloso *et al.* 1992; Holcombe 2006), although the reasons for this have not been explained.

2.10.2 Effect of an endoscope on respiratory parameters during exercise

Three studies have been undertaken to investigate the effect of an endoscope on respiratory parameters during exercise. Art *et al.* (1990) reported a 17.7% decrease in airflow during maximal exercise when a length of tubing of similar diameter to an endoscope was placed in the nasal passage. However, Franklin (2002) compared airflows and tidal volume passing through each nostril in five horses on two occasions, once with and once without an endoscope in place. The presence of the endoscope had no significant effect on airflow or tidal volume during high speed exercise. Also it has been reported that proximal airway pressure measurements in exercising horses are unaffected by the presence of an endoscope (Rehder 1992 cited by Ducharme *et al.* 1994 and Rehder *et al.* 1995). It is therefore unclear whether the endoscope does or does not affect upper airway mechanics. It is uncertain whether the effect on upper airway mechanics is smaller than can be measured by the accuracy of the equipment. One review article (McCann 2000) suggested that the presence of the endoscope in the airway during exercise may induce dynamic URT obstructions. Clearly this does not happen in all horses as numerous horses have been confirmed to have normal URT function during treadmill endoscopy. However with the absence of a better testing method, it is not possible to assess whether in some individuals the presence of the endoscope could induce an abnormality in a normal horse.

2.10.3 Position of endoscope

There may be some variation in endoscope positioning between the studies. Lane *et al.* (2006a) suggested that the endoscope be positioned at the level of the openings of the auditory tube diverticula. Parente *et al.* (2002) and Martin *et al.* (2000) suggest that the endoscope be positioned just caudal to the openings of the auditory tubes. Both of these positions should allow the apex of the epiglottis, the caudal soft palate and arytenoid cartilages to be clearly visible (Tan *et al.* 2005).

However some clinicians position the endoscope more caudally whereby the tip of the endoscope is positioned above the epiglottis. In these circumstances neither the tip of the epiglottis nor the soft palate can be adequately visualised. Although it would be possible to diagnose DDSP, it would not be possible to diagnose PI or other forms of pharyngeal wall collapse.

2.11 Discussion

Several approaches to making a diagnosis of dynamic palatal dysfunction have been described. Although history and presenting complaint are not truly diagnostic tests, they were included in this review as many horses have a diagnosis based on history alone or in conjunction with resting endoscopy findings.

The evidence base for the diagnostic methods is weak. Most of this chapter was simply descriptive and only a few diagnostic accuracy studies have been performed. Generally the caseloads within these studies are appropriate to what would be seen in clinical practice. However, there are differences in the prevalence of this condition between sport horses and racehorses and there was some variation in the results between the populations. All of the studies appear to be retrospective studies performed on hospital case records and there is no evidence that any of the studies was conducted in a blinded manner. With the use of retrospective case records it is unclear how accurately the records had been maintained. Furthermore, as highlighted there are question marks over the use of treadmill endoscopy as the gold standard to compare other diagnostic tests.

This review has shown that definitive diagnosis of palatal dysfunction can be problematic. Generally these studies suggest that respiratory noise, resting endoscopy findings or both in conjunction may be unreliable in predicting dynamic events that occur during exercise. A more general history of 'abnormal noise' was not specific enough to be used to determine a diagnosis of palatal dysfunction. However the specificity of 'gurgling' was much higher, and is more suggestive of this condition.

Although the studies showed that DDSP during resting endoscopy had a high specificity for DDSP during exercise, the sensitivity was either low or with high confidence intervals. As a result resting endoscopy alone would result in very high levels of false negative cases.

Greenhalgh (2010) suggested that tests with false negative rates this high are more likely to mislead clinicians than assist the diagnosis if the target disorder is actually present. However the LR's suggest the test does have some value. For example, using the data from Lane *et al.* (2006b) (figure 2.4, table 2.6) the pre-test probability of having DDSP is 40%. The post test probability of a horse having DDSP during exercise if the horse exhibits DDSP at rest is 56%. Despite this it should be noted that studies based on resting endoscopy would include only a small subset of cases, and it is unclear whether these are representative of the wider population of horses experiencing DDSP during exercise, or whether these cases might be more severely affected. It appears that other resting endoscopy findings such as epiglottic appearance and soft palate ulceration, laryngeal ultrasound and spectral analysis also have limitations. Furthermore, the diagnostic techniques used must also enable a definitive diagnosis of other URT obstructions to be made.

The inaccuracy of resting endoscopy is not surprising when one considers the dramatic increases in airflow and airway pressure changes that occur during exercise. In many horses airway obstruction will only occur during strenuous exercise when airflow and the collapsing forces are at their peak. Furthermore it is thought that a combination of neuromuscular fatigue and strong negative inspiratory pressures are required for URT obstructions to become manifest (Weishaupt 2005). Even when it is possible to generate similar negative pressures at rest i.e. with nasal occlusion, the low respiratory rate means that there is no fatigue of the upper airway musculature which likely explains why this technique is also unable to replicate the conditions of exercise.

It has been suggested that in an ideal world all equine athletes with poor performance would be evaluated by high speed treadmill endoscopy (Lane *et al.* 2006b). The losses sustained as a result of incomplete or incorrect diagnoses may be considerable. Not only should the cost of inappropriate treatments be taken into consideration, but also the cost of convalescence, futile training, additional surgeries, loss of earnings and horse devaluation (Lane *et al.* 2006b). Furthermore the welfare implications of large numbers of horses undergoing inappropriate surgeries are important.

Although treadmill endoscopy is considered to be the most appropriate diagnostic method, there are limitations. Of the known URT abnormalities, DDSP is the most likely not to be reproduced on a high speed treadmill despite circumstantial evidence of the condition under field conditions

(Parente and Derksen 2006). Currently it may not be possible to be sure that a horse does not have DDSP.

A low cost widely available diagnostic tool would be invaluable for the diagnosis of URT collapse, and would significantly improve equine welfare. The development of portable endoscopes for use in the field (~overground endoscopy) (Burn *et al.* 2006), may offer a lower cost diagnostic technique with much wider availability. In addition this may overcome the disadvantages of treadmill testing not replicating racing.

Often no single, clear cut diagnostic tests exist that reliably distinguish 'normal' from 'abnormal'. The general principle – do several tests and combining them – is a long standing rule of thumb in clinical practice (Greenhalgh 2010) and would be appropriate for this condition. Currently incorporating information from the history, resting endoscopy and exercising endoscopy would appear most useful in clinical practice. The addition of laryngeal ultrasound does not appear to be warranted for establishing a diagnosis of palatal dysfunction in clinical practice, based upon the current evidence. However, it may provide valuable information for other laryngeal obstructions and some authors have incorporated this technique as a routine procedure for investigation of upper airway disorders (Garrett 2010). Future publications on diagnostic accuracy should be written using the STARD (Standards for Reporting of Diagnostic Accuracy) framework and guidelines (Bossuyt *et al.* 2003). In human medicine there has also been rapid research in recent years in the development of clinical prediction rules (Greenhalgh 2010). Clinical prediction rules quantify the contribution of symptoms, clinical signs and available diagnostic tests and categorise patients according to the probability of having the target disorder (Falk and Fahey 2009). This would also be of value to undertake in a large scale study for this condition.

In many circumstances diagnostic tests are not solely about obtaining diagnosis. They may also provide information about the severity of the condition, the prognosis, the likely responsiveness to therapy and the actual response to therapy (Guyatt *et al.* 2006). PI is generally considered to be a milder form of palatal dysfunction than DDSP (Lane *et al.* 2006a; Barakzai and Dixon 2011), however there is no grading system or advice on the assessment of severity for either PI or DDSP. Furthermore, there is also no published information to interpret the prognosis or likely responsiveness to therapy for horses with palatal dysfunction.

Chapter 3 Aetiopathogenesis of palatal dysfunction: a critical review of the evidence

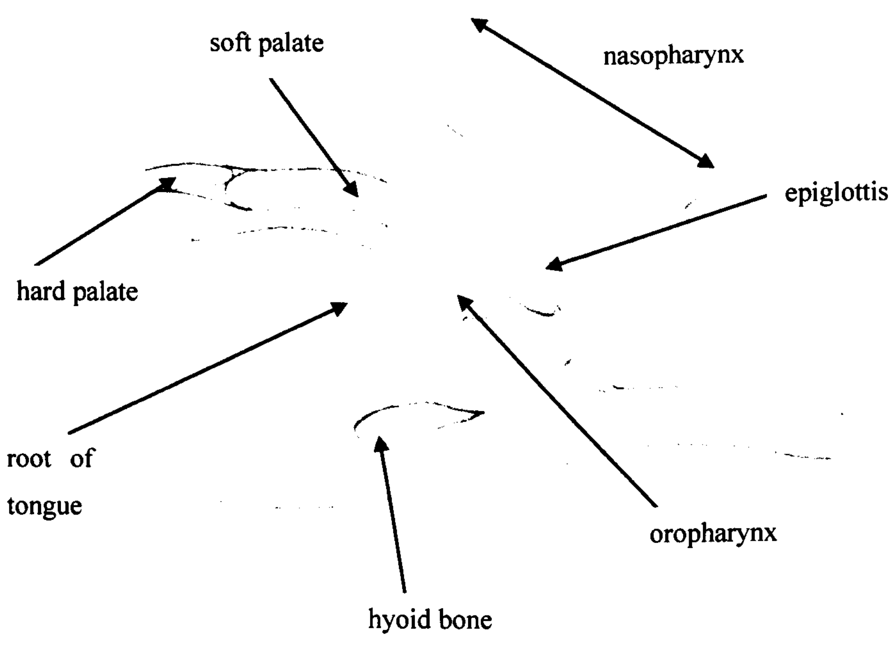
3.1 Introduction

It is important that the aetiopathogenesis of a condition is well understood if effective treatment and prevention strategies are to be developed (Haynes 2006a). Therefore the aim of this chapter was to critically assess the literature on the aetiopathogenesis of dynamic palatal dysfunction. Palatal dysfunction has also been reported during sleep in man (snoring and obstructive sleep apnea (OSA)) and at rest and during exercise in brachycephalic dogs (as part of brachycephalic syndrome). Substantial research has been undertaken studying normal and abnormal pharyngeal function to better understand OSA and the relevant literature from human research and other species will be included here where applicable. A number of hypotheses have been proposed regarding the aetiopathogenesis of palatal dysfunction. These relate to both intrinsic factors affecting the soft palate itself and extrinsic factors associated with the surrounding tissues. Before investigating each of these in detail it is important to first review the normal anatomy and function of the soft palate and nasopharynx.

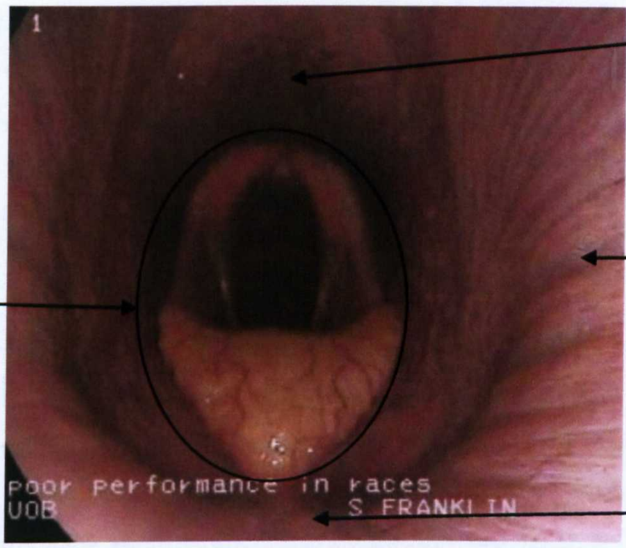
3.2 Upper airway anatomy

The nasopharynx is a musculo-membranous tube, of which the soft palate makes up the floor (figures 3.1 and 3.2). The anatomy of the equine nasopharynx is different to that of many other mammalian species, in that the horse is an obligate nasal breather, as a result of the relationship between the larynx and the soft palate. In other athletic species (such as man and greyhounds) a switch from nasal to oral breathing occurs during exercise in order to avoid the high resistance to airflow incurred by nasal breathing. However, the long sub-epiglottic position of the soft palate of the horse (figure 3.1) means that the horse continues to nasal breathe throughout exercise. It has been suggested that this anatomic arrangement may have olfactory advantages to detect predators during feeding, an important defence strategy in wild horses (Negus 1929). In the horse, displacement of the soft palate dorsally is a normal occurrence only during swallowing and vocalization.

The mean length of the soft palate, measured post-mortem, in Thoroughbreds is 134mm (±12mm) (Richardson *et al.* 2006). The rostral soft palate contains a broad tendinous aponeurosis, which extends caudally from the hard palate, onto which the palatal musculature attaches. The palatine aponeurosis extends up to 40% of the overall length of the soft palate, although its exact length may vary between individuals (Richardson *et al.* 2006). The muscular tissue is located dorsal to the glandular tissue which makes up the bulk of the soft palate (Richardson *et al.* 2006). The caudal free border of the soft palate continues dorsally on either side of the larynx and unites dorsal to the larynx forming the palatopharyngeal arch.

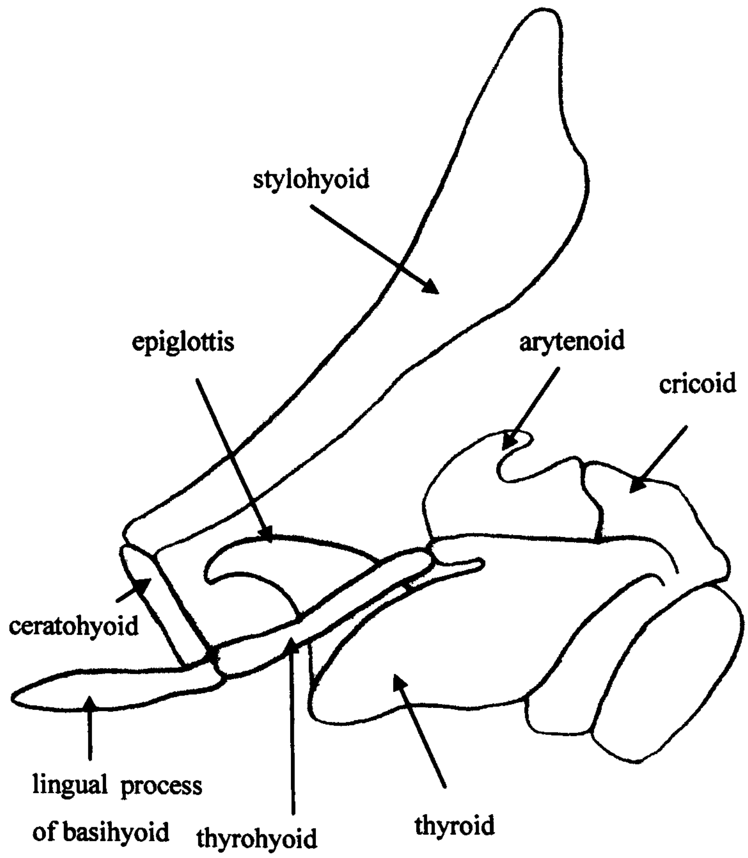


3.1 Schematic diagram of a sagittal section of the pharyngeal region in the horse. The sub-epiglottic position of the soft palate can be seen separating the nasopharynx from the oropharynx.



3.2 Endoscopic view of the larynx within the nasopharynx. The soft palate makes up the floor of the nasopharynx.

The hyoid apparatus functions to support the tongue, nasopharynx and larynx and consists of paired stylohyoid, ceratohyoid and thyrohoid bones, a single basihyoid bone and a lingual process (figure 3.3). The stylohyoid bone articulates with the base of the skull at the petrous temporal bone. The thyrohyoid articulates with the thyroid cartilage of the larynx and the lingual process is embedded in the root of the tongue. The larynx is composed of epiglottic, thyroid, cricoid and arytenoid cartilages (figure 3.3).



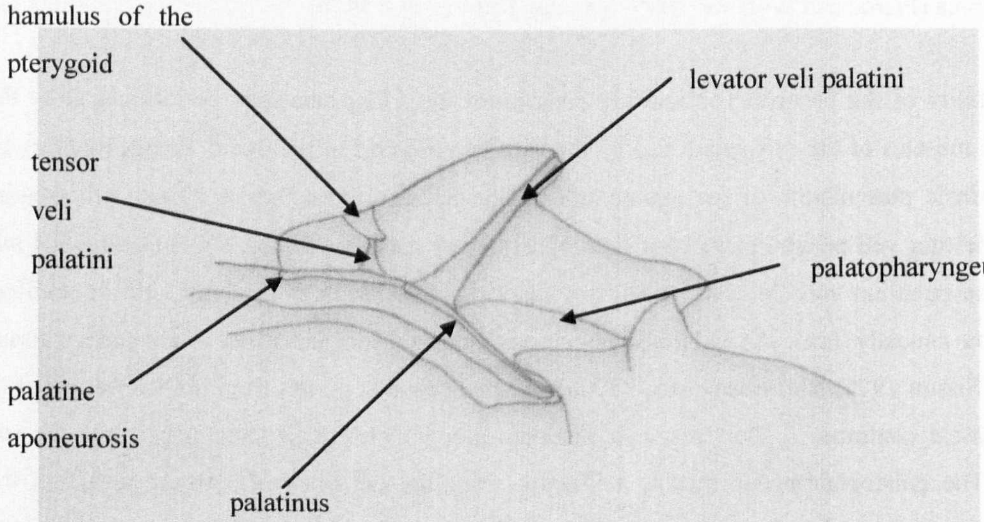
3.3 Schematic diagram of laryngeal cartilages and hyoid apparatus

3.3 Functional stability of the nasopharynx

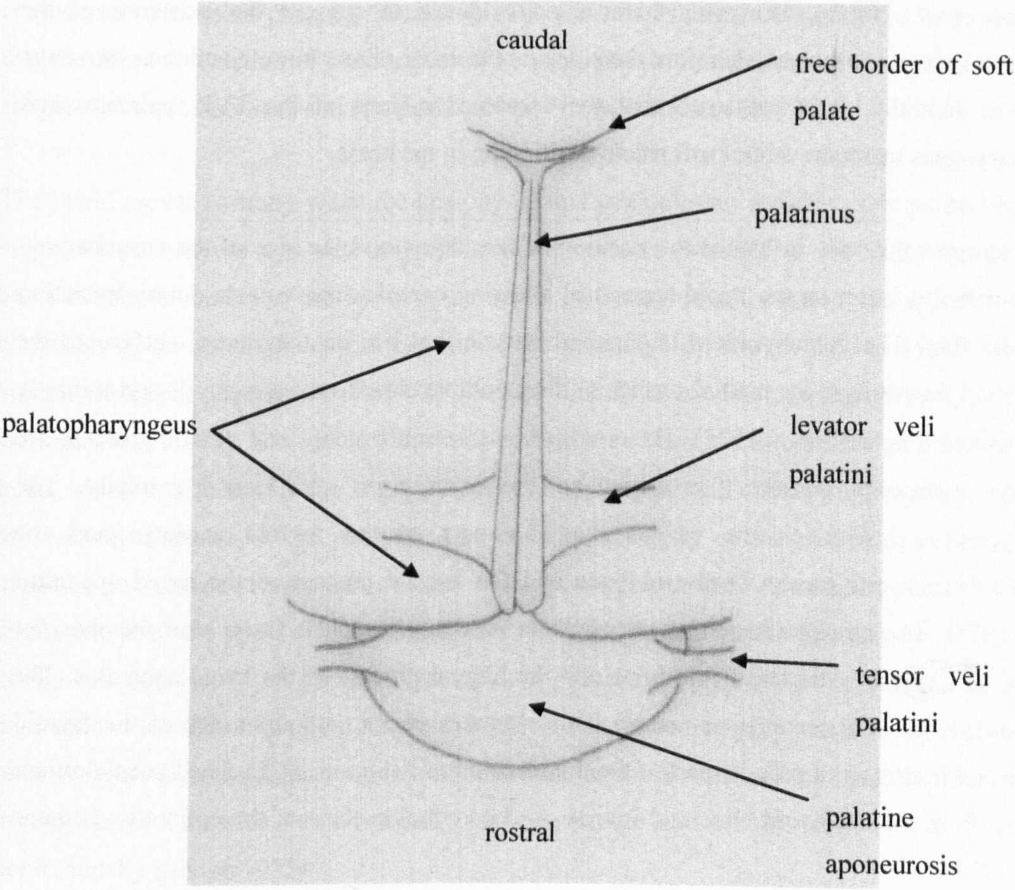
The nasopharynx is the only part of the upper airway which has no bony or cartilaginous support and requires muscular activity to maintain patency. In man, the activity of several upper airway muscles is increased during inspiration, thus stiffening and dilating the upper airway to counteract the collapsing influence of negative airway pressure (van Lunteren 1993). Studies have shown that the tendency for the upper airway to collapse is inversely related to the activity of the upper airway dilator muscles (Arens and Marcus 2004). Thus in OSA the combined forces of the upper airway dilating muscles are not sufficient to overcome the negative inspiratory pressure created by the thorax (Svanborg 2005).

In other species activation of upper airway muscles during exercise is as a result of mechanoreceptors within the upper airway mucosa and/ or as a result of chemical drive (Van der Touw *et al.* 1994ab). Mechanoreceptors particularly respond to negative airway pressure (Pierce and Worsnop 1999; Van der Touw *et al.* 1994b). Chemical drive is the response to hypoxia and hypercapnia (Pierce and Worsnop 1999; Van der Touw *et al.* 1994b).

The stability of the nasopharynx and the position of the soft palate may be influenced by the intrinsic muscles of the soft palate and by the extrinsic muscles of the hyoid, tongue and larynx. The intrinsic musculature of the equine soft palate includes the palatinus, tensor veli palatini (TVP), levator veli palatini (LVP) and palatopharyngeus muscles (Sisson 1975) (figures 3.4 and 3.5). The palatinus muscle consists of two fusiform muscles that lie either side of midline, extending caudally from the palatine aponeurosis and are surrounded by a connective tissue sheath (Sisson 1975; Richardson *et al.* 2006). A small bundle arising from the lateral aspect of each muscle continues a short distance caudodorsally into the palatopharyngeal arch (Sisson 1975). The palatopharyngeus muscle originates from the palatine aponeurosis lateral to the palatinus muscle and further fibres attach ventrally along the length of the connective tissue sheath of the palatinus muscle (Sisson 1975; Richardson *et al.* 2006). The palatopharyngeus muscle travels caudally along the lateral wall of the nasopharynx to the pharyngeal raphe, forming part of the superior constrictor muscle group. In the horse the palatinus and palatopharyngeus are thought to control the caudal half of soft palate (Holcombe *et al.* 1998). Contraction of the palatinus muscle is thought to shorten the soft palate and contraction of the palatopharyngeus shortens the nasopharynx (Sisson 1975). In the horse it is presumed that the combined action depresses the soft palate (Holcombe *et al.* 1998), however in other species it is thought that the muscle may depress or elevate the soft palate (Holcombe *et al.* 2007). The levator veli palatini muscles arise from the petrous temporal bone, passing rostrally then ventrally in the pharyngeal walls. The muscle turns medially to insert into the soft palate, in which it spreads out above the glandular layer and ventral to the palatinus muscle forming a sling-like structure (Sisson 1975; Richardson *et al.* 2006). Contraction of the levator veli palatini elevates the middle portion of the soft palate (Kogo *et al.* 1997). The tensor veli palatini is a flat fusiform muscle that travels with the levator veli palatini along the lateral walls of the nasopharynx and the lateral lamina of the guttural pouch. Its tendon is reflected around the hamulus of the pterygoid bone, where it is lubricated by a bursa (Sisson 1975). The tendon then ramifies in the palatine aponeurosis. Contraction of the tensor veli palatini muscle is thought to tense the palatine aponeurosis (Sisson 1975) and depresses the rostral soft palate toward the tongue (Holcombe and Ducharme 2007).



3.4 Schematic diagram of the nasopharynx showing the location of the intrinsic musculature



3.5 Schematic diagram of the intrinsic soft palate musculature viewed from dorsally

In other species, soft palate position plays a role in oronasal partitioning of airflow during times of increased ventilation, such as exercise. Ventral positioning of the soft palate permits nasal airflow and dorsal positioning of the soft palate permits oral airflow. In man the position of the soft palate is thought to be under active muscular control rather than solely gravity as the negative pharyngeal pressure during inspiration would tend to pull the soft palate dorsally (Rodenstein and Stanescu 1984). It was suggested that during quiet breathing, when there is predominately nasal airflow, the activity of the palatoglossus muscle (which directs the soft palate caudally and ventrally) predominates over that of the LVP (which tends to pull the soft palate in a cranial and dorsal direction). In the horse folds of mucous membrane pass dorsally from the base of the tongue to form the palatoglossal arches, which attach the tongue to the soft palate (Sisson 1975, Cornelisse *et al.* 2001b). However, there is no evidence to suggest the existence of the palatoglossal muscle in horses, therefore there appears to be no direct muscle action to move the soft palate ventrally. It is presumed that the combined actions of the TVP, palatinus and palatopharyngeus maintain ventral soft palate positioning in the horse.

The hyoid apparatus may influence the position of the larynx and the size of the nasopharynx. Multiple muscles insert on the hyoid apparatus, allowing complex movements during breathing and swallowing. The geniohyoideus is a paired muscle that lies on the ventral surface of the tongue. It originates from the medial surface of the mandible close to the symphysis and it inserts on the basihyoid bone (Sisson 1975). The omohyoideus, sternohyoideus and sternothyroideus are accessory respiratory muscles that insert on the manubrium and extend cranially. The sternothyroideus inserts on the caudal abaxial aspect of the thyroid cartilage and the sternohyoideus inserts on the basihyoid bone and the lingual process of the hyoid apparatus (Sisson 1975). The omohyoideus muscles originate on the subscapular fascia near the shoulder joint and also insert on the basihyoid bone and the lingual process of the hyoid apparatus. The thyrohyoideus is a flat rectangular muscle that originates on the lateral surface of the thyroid cartilage and inserts on the caudal part of the thyrohyoid bone (Sisson 1975). The hyoepiglotticus originates from the basihyoid bone and inserts on the ventral surface of the epiglottic cartilage (Sisson 1975).

There are three extrinsic tongue muscles: genioglossus, hyoglossus and styloglossus. The genioglossus originates from the medial surface of the mandible, just caudal to the symphysis. Some muscle fibres radiate rostrally toward the tip of the tongue, some dorsally, and some distally toward the root of the tongue (Sisson 1975). The hyoglossus is a wide flat muscle that lies in the lateral part of the base and body of the tongue (Sisson 1975). It originates from the lateral aspect of the basihyoid bone and from the stylohyoid and thyrohyoid bones (Sisson 1975). The styloglossus originates from the lateral surface of the stylohyoid bone and travels along the lateral aspect of the tongue. Near the tip of the tongue the paired muscle meets and ramifies with the intrinsic musculature (Sisson 1975). Contraction of genioglossus causes protrusion and depression of the tongue (Oliven *et al.* 2007). In man genioglossus is considered the primary upper airway dilator muscle (Pierce and Worsnop 1999; Cheng *et al.* 2008; Jordan and White 2008). Although genioglossus is thought to reduce pharyngeal resistance and collapsibility more than all other upper airway dilators, it's effects are far greater when contraction occurs in conjunction with other pharyngeal muscles (Oliven *et al.* 2007). In horses it has been suggested that the depressive action of contraction of the genioglossus muscle, rather than protrusion of the tongue that most stabilizes and dilates the airway (Cornelisse *et al.* 2001b).

The hyoid moves rostrally when the geniohyoid and genioglossus muscles contract and caudally when the sternohyoid and sternothyroid muscles contract (Morello *et al.* 2008; Sisson 1975). Most of the movement of the hyoid apparatus is in the stylohyoid-ceratohyoid articulation, and extension of the joint (cranial movement of the ceratohyoids) moves the basihyoid bone in a ventral direction (Roberts *et al.* 1984; Van de Graaff *et al.* 1984; Wiegand and Latz 1991; Derksen *et al.* 1999). The vertical distance between the base of the cranium and the basihyoid bone, which is affected by the angle between the stylohyoid and ceratohyoid bones, determines the vertical diameter of the pharynx. The combined activity of the rostral and caudal hyoid musculature causes extension of the stylohyoid-ceratohyoid articulation and a ventral displacement of the hyoid (Jordan and White 2008) and an increase in the diameter and stability of the nasopharynx (Van de Graaff *et al.* 1984; Becker *et al.* 1999). Thyrohyoideus muscle contraction also moves the hyoid bone caudally or the larynx rostrally and dorsally. If the hyoid bone is fixed, thyrohyoideus contraction moves the larynx rostrally, if the hyoid is free to move, thyrohyoideus acts with sternohyoideus, sternothyroideus and omohyoideus to draw the hyoid bone caudally (Sisson 1975).

Movements of the hyoid and larynx during the respiratory cycle have not been well studied in the horse. In man and other species it is thought that the hyoid bone moves anteriorly (ventrally) during inspiration (Mitchinson and Yoffrey 1947; Rothstein *et al.* 1983, Van de Graaff *et al.* 1984; van Lunteren 1990). It was suggested that the extent of anterior movement may be quite substantial, in contrast the cranial caudal movement of the hyoid arch is small and variable in direction during breathing (van Lunteren 1990). In exercising horses, Ducharme (1992) originally proposed that the larynx moved caudally during expiration. However, more recently the same group suggested that the hyoid and larynx move in unison caudally during inspiration and rostrally during expiration (Tsukroff *et al.* 1998). This latter observation is in accordance with van Lunteren (1990) and Van de Graaff (1988) who suggested that in all mammalian species caudal movement of the tracheobronchial tree during inspiration imparts a caudal force to the larynx, which is transmitted to the hyoid arch via the thyrohyoid muscle. This caudal inspiratory movement of the trachea is thought to have a dilating effect on the upper airway independent of contraction of the upper airway muscles.

In the horse the following muscles, which may have a role in pharyngeal patency, have been confirmed to have respiratory related activity: genioglossus, geniohyoideus, hyoepiglotticus, omohyoideus, sternohyoideus, sternothyroideus, thyrohyoideus, stylopharyngeus, palatinus and palatopharyngeus muscles (table 3.1) (Holcombe *et al.* 2002; Tessier *et al.* 2005; Holcombe *et al.* 2007; Morello *et al.* 2008). LVP and TVP have respiratory related activity in other species, but have not yet been studied in the horse (Tangel *et al.* 1995, Van der Touw *et al.* 1994 ab).

Table 3.1 Shows the pharyngeal dilator muscles studied in horses

Muscle	Predominant activity	Effect of exercise	Reference
Hyoepiglotticus	Inspiration	Increases	Holcombe *et al.* 2002
Hyoepiglotticus	Inspiration	Increases	Morello *et al.* 2008
Stylopharyngeus	Inspiration	Increases	Tessier *et al.* 2005
Geniohyoid	Expiration	Increases	Morello *et al.* 2008
Genioglossus	Expiration	Increases	Morello *et al.* 2008
Thyrohyoideus	Expiration	None	Morello *et al.* 2008
Sternohyoid	Expiration	None	Morello *et al.* 2008
Sternothyroid	Inspiration	None	Morello *et al.* 2008
Omohyoid	Continuous	None	Morello *et al.* 2008
Palatinus	Expiration	Increases	Holcombe *et al.* 2007
Palatopharyngeus	Expiration	Increase	Holcombe *et al.* 2007

The palatinus, palatopharyngeus, geniohyoideus, sternohyoideus, thyrohyoideus and genioglossus muscles have been shown to have predominately expiratory activity in the horse (Holcombe *et al.* 2007, Morello *et al.* 2008). The palatinus and palatopharyngeus showed activity throughout the breathing cycle, but activity increased towards the end of inspiration and peaked early to mid expiration (Holcombe *et al.* 2007). For the geniohyoid, genioglossus and sternohyoideus primarily expiratory activity was seen with peak activity immediately preceding inspiration (Morello *et al.* 2008). The thyrohyoideus had expiratory activity and in most horses was quiescent during inspiration (Morello *et al.* 2008). In contrast, in other species these muscles commonly have predominantly inspiratory activity (van Lunteren 1990; Brancatisano *et al.* 1996; Van der Touw *et al.* 1994ab; Pierce and Worsnop 1999; Holcombe *et al.* 2007; Jordan and White 2008). The typical pattern of electrical activity in upper airway dilator muscles is that discharge commences before the onset of inspiratory flow, activity then rises rapidly to a peak at early or mid-inspiration followed by a plateau or downward sloping phase during the remainder of inspiration and becomes more quiescent or totally quiet during expiration (Van Lunteren 1990; van der Touw *et al.* 1994b). The muscle activity just prior to the onset of inspiration is thought to enlarge and stabilise the upper airway prior to the development of subatmospheric inspiratory pressures (Van der Touw *et al.* 1994b; Pierce and Worsnop 1999; Series 2002). Van der Touw *et al.* (1994a) found that dogs show increased inspiratory activation of the soft palate muscles in response to negative upper airway pressure. However two other studies found that predominately expiratory activity was seen in soft palate muscles in dogs in response to hypoxic hypercapnia and CO_2 administration (Van der Touw *et al.* 1994b; Amis *et al.* 1996a). It was suggested that the dual inspiratory expiratory nature of the soft palate muscles in dogs may reflect the role of the soft palate in controlling oronasal flow partitioning during inspiration and expiration (Van der Touw *et al.* 1994b). Electromyography studies suggest that the pharyngeal constrictors (as opposed to the pharyngeal dilators described above) have activity during expiration (Kuna and Vanoye 1999). The expiratory activity of the pharyngeal constrictors has been suggested to aid return of the pharyngeal structures to their resting position after their caudal displacement during inspiration (Kuna and Vanoye 1999). It is unclear why in the horse, muscles known to have inspiratory activity in other species would have predominately expiratory activity. Holcombe *et al.* (2007) suggested that as DDSP was considered an expiratory obstruction, these muscles would have expiratory activity. However expiratory obstruction only occurs once displacement has occurred and the URT must maintain patency in the face of the large negative inspiratory pressures that occur during exercise. It is unclear how patency could be maintained during inspiration without inspiratory muscle activity. Holcombe *et al.* (2007) also proposed that the expiratory activity may relate to breathing methodology of the horse but this was not further elaborated. Most of the muscles shown to have expiratory activity in the horse act to reposition the larynx or pharynx more rostrally, perhaps the function is similar to that described by Kuna and Vanoye (1999) to return the larynx and pharynx to the resting position following their caudal displacement during inspiration.

3.4 Proposed causes of dynamic palatal dysfunction

3.4.1 Intrinsic factors

3.4.1.1 Soft palate length

An excessively long soft palate was one of the earliest proposed mechanisms for DDSP (Quinlan *et al.* 1949) and has also been reported in brachycephalic dogs (Wykes 1991; Hendricks 1992). In brachycephalic breeds the skull bone shortening is not paralleled by a shortening of the soft palate, thereby resulting in a relatively longer soft palate (Harvey 1989). There have been no studies investigating this in the horse and as yet there is no evidence to support this proposal. However, it would seem unlikely in Thoroughbreds as selective breeding for shorter skulls has not occurred.

3.4.1.2 Soft palate weakness

In the normal horse the factors that maintain ventral position of soft palate must exceed the negative pharyngeal pressures that occur during inspiration which would act to lift the soft palate dorsally. It was proposed that DDSP might occur when excessively negative pharyngeal pressures were encountered (Seeherman *et al.* 1992; Rehder *et al.* 1995). However this was refuted in the study by Rehder *et al.* (1995) in which the degree of negative pharyngeal pressure did not have a direct correlation with occurrence of DDSP. This study was based on only 19 horses, of which 7 displaced associated with swallowing and 10 displaced on slowing down from the highest speed step. Ideally the study would be based on horses that displace during strenuous exercise only and that the displacement was not associated with a swallow. In 6 horses in which DDSP occurred at steady speed the pharyngeal inspiratory pressures immediately prior to displacement were significantly less negative than the peak pressures in that horse (Rehder *et al.* 1995). This suggests that affected horses are not able to maintain a ventral soft palate position in the face of 'normal' pressures that occur during exercise. Thus factors associated with the soft palate itself were suggested to be influential in the pathogenesis.

It has been proposed that soft palate position is maintained due to stiffness or strength of the soft palate, although the variables that determine this are not well investigated (Franklin 2009). Factors such as the distribution of tissue types within the soft palate may be involved (Franklin 2009). Cook (1981) proposed that DDSP affected horses had soft palates lacking in glandular tissue, however this has not been investigated. In OSA patients the soft palate undergoes connective tissue alterations leading to increased elastance. Therefore the degree of shortening of the soft palate for a given muscle contraction was significantly less than normal (Series *et al.* 1999; Kimoff 2007). The intrinsic musculature also likely plays an important role in determining the stiffness of the soft palate (Franklin 2009) and weakness of the palatal musculature could result in an inability of the soft palate to withstand the airway pressures during exercise. Muscle weakness might occur as a result of chronic denervation, myopathy, myositis, alterations in muscle fibre type, premature fatigue through genetic variations in muscle mass or muscle fibre type or through inappropriate training.

3.4.1.2.1 Physiological factors

Anderson (1984) first reported the muscle fibre types and their proportions and the findings were confirmed in subsequent studies. Holcombe and Ducharme (2004) reported 5-25% type I fibres in the palatinus, and 10-25% type I fibres in the palatopharyngeus. Hawkes *et al.* (2010) also confirmed that the soft palate muscles have a low proportion of type I muscle fibres: 7% in the palatinus, 4-7% in the palatopharyngeus, 8% in the LVP and 17% in the TVP. Similarly, the palatopharyngeus and uvula muscles contain two of the highest proportions (86-87%) of type II fibres ever reported for human muscles (Stål and Lindman 2000). In contrast the LVP and TVP contain approximately 50-70% type I fibres (Moon *et al.* 1998, Stål and Lindman 2000).

It has been shown in several studies that muscles involved in pharyngeal dilation have a greater proportion of type II muscles and, hence, are less fatigue-resistant than the main respiratory muscle, the diaphragm (Dick and Van Lunteren 1990; Van Lunteren *et al.* 1990; Bracher *et al.* 1997). In dogs it was also shown that the main upper airway dilator muscles which participate regularly in respiratory activity are structurally identical to those of neighbouring upper airway muscles that do not dilate the pharynx and have no respiratory role (Bracher *et al.* 1997). The authors suggested that under normal circumstances, upper airway dilator muscles exhibit only low intensity inspiratory activation and may not be specifically adapted for increased, chronic respiratory loads, which require high endurance. It was suggested in man that when detrimental anatomical variations are present in the upper airway, such as occurs in obstructive sleep apnea, the respiratory demands on the upper airway dilator muscles are increased, and therefore these muscles may approach the limit of their endurance capabilities (Bracher *et al.* 1997).

Furthermore increased levels of muscle activity are capable of inducing structural damage in muscle fibres (Petrof *et al.* 1994). In this regard, a so-called 'overuse' syndrome has been described in muscle subjected to unaccustomed or heavy use. In dogs it has also been proposed that chronic load leads to myopathic changes which may ultimately impair the ability of these muscles to maintain pharyngeal patency (Petrof *et al.* 1994).

Skeletal muscles are known to change their fibre composition in response to different functional demands. This adaptive plasticity enables muscle fibres to switch from one type to another, in response to altered chronic mechanical needs. Vincent *et al.* (2002) showed that chronic endurance exercise in rats is associated with a fast-to-slow shift in MyHC phenotype together with an increase in both oxidative and anti-oxidant capacity in the sternohyoid and digastricus muscle but not in the omohyoid and genioglossus muscles. It is unclear whether the upper airway musculature changes in response to athletic training in the horse. Anecdotally, palatal dysfunction in young (2 year old) horses is suggested to improve with increases in fitness or training.

As a result of domestication, racehorses have to withstand exercise intensities that they were not necessarily evolved for. With increasing speeds, minute ventilation increases almost linearly, from 60 - 80 l/min at rest to 1800 l/min during strenuous exercise (Art and Lekeux 1993; Butler *et al.* 1993). These high airflows are generated primarily by diaphragmatic movement which produces pleural pressure decreases to -30 cmH_2O during inspiration and increases to +30 cmH_2O during expiration (Slocombe *et al.* 1991; Ainsworth *et al.* 1996). During gallop exercise pharyngeal inspiratory pressures of -20 to -26 cmH_2O and expiratory pressures of 10 to 24 cmH_2O have been recorded (Ducharme *et al.* 1994). Therefore under racing conditions the soft palate and pharyngeal dilators have to withstand high inspiratory pressures for relatively prolonged duration. The demands of racing may be greater than the intrinsic soft palate muscles with low proportion of type 1 muscle fibres can withstand. It is clear from the clinical situation that fatigue may play a role. Typically DDSP occurs at the end of races or the end of the exercise test (Ahern 1999b; Franklin 2002).

However simply assessing fibre type may not be sufficient to make claims of the endurance capacity of a muscle. A large number of other parameters, including enzyme profile and metabolic properties, are known to affect muscle performance (Bracher *et al.* 1997). Despite the type II fibre predominance in the palatopharyngeus and uvula, these muscles showed a richer capillarisation than previously reported for human limb muscles and a high mitochondrial enzyme activity and it was suggested that these fibres have a large capacity for aerobic metabolism and thereby a high fatigue resistance (Stål and Lindman 2000). These factors have not been assessed in equine palatal musculature.

3.4.1.2.2 Pathological factors

The LVP elevates the soft palate during swallowing and during oral breathing in nonobligate nasal breathers (Derksen *et al.* 1999). Cook (1981) proposed that inappropriate contraction of LVP may be involved in DDSP, however this has not been investigated. Contraction of the tensor veli palatini muscle is thought to tense the palatine aponeurosis (Sisson 1975) and depresses the rostral soft palate toward the tongue (Holcombe and Ducharme 2007). Dysfunction of this muscle was proposed to be involved in the pathogenesis of DDSP. However although bilateral tenectomy of the TVP did result in billowing of the rostral soft palate during exercise, DDSP did not occur (Holcombe *et al.* 1997a). In other species electrical stimulation of TVP decreased airway collapsibility (McWhorter *et al.* 1999), however the role of this muscle is probably small (Honjo *et al.* 1979; McWhorter *et al.* 1999) and it has been suggested the coordinated activation of the palatopharyngeal muscles is required to adequately influence upper airway collapsibility (McWhorter *et al.* 1999). Most research in horses and other species has focused on the palatinus (called musculus uvulae in man) and the palatopharyngeus muscles.

Dysfunction of the palatinus and palatopharyngeus muscles or their innervations via the pharyngeal branch of the vagus has been proposed to cause instability of the caudal soft palate and lead to DDSP (Holcombe *et al.* 1998). Diminished muscle activity of the palatinus muscle has been detected in horses prior to DDSP (Holcombe and Ducharme 2004). However, the number of horses studied is very low. Local anaesthetic of the pharyngeal branch of vagus within the guttural pouches caused DDSP. However the DDSP was persistent and was also associated with dysphagia, which is unlike the clinical scenario. It was suggested that this nerve may be damaged more distally than within the guttural pouch (Holcombe *et al.* 1998). Prior to ramifying in the pharyngeal plexus this nerve lies close to the retropharyngeal lymph nodes within the guttural pouch, and it was proposed that the nerve may be damaged by lymphadenopathy, inflammation or infection (Holcombe *et al.* 1998). Anecdotally it is often suggested that palatal dysfunction occurs following an upper respiratory tract infection (Ducharme 2001; Franklin 2002; Holcombe and Ducharme 2007). However there has been little objective evidence so far that confirms the role of infection or inflammation. The prevalence and severity of pharyngeal lymphoid hyperplasia is reported to decrease with increasing age (Saulez and Gummow 2009) and the prevalence of DDSP is reported to decrease with increasing age (Lane *et al.* 2006a). Adenotonsillar hypertrophy is also considered to be a major factor in the pathophysiology of OSA in children (Goldbart *et al.* 2007). It has been suggested that some viral respiratory infections lead to long term alterations in the neuroimmunomodulatory pathways of lymphoid tissue, which subsequently lead to accelerated proliferative responses and are thus associated with an increased prevalence of OSA (Goldbart *et al.* 2007).

Anderson (1984) reported that the general histological features of equine palatal muscles were similar to those of the laryngeal muscles. However, the most notable difference was reported to be the absence of fibre type grouping in soft palate musculature which was so commonly demonstrated in the laryngeal muscles (as a result of recurrent laryngeal neuropathy). But it was also reported that the palatal muscles contained certain features which were considered to be associated with denervation and reinnervation when they occurred in laryngeal muscles. Marked variation in fibres size and well developed endomysial connective tissue appeared to be a feature of all the palatine muscles and these histological features were just as likely to be present in left or right muscles and were seen in the muscles from horses of all ages.

The most recent study by Hawkes *et al.* (2010) revealed very similar findings to Anderson (1984). Considerable variability in muscle fibre size was observed. The caudal palatopharyngeus contained marked variation in fibre size and shape and increased epimysial connective tissue. Although these findings were considered unusual morphological features, they were observed in all 6 horses and similar to Anderson (1984) were considered to be a normal feature of this muscle.

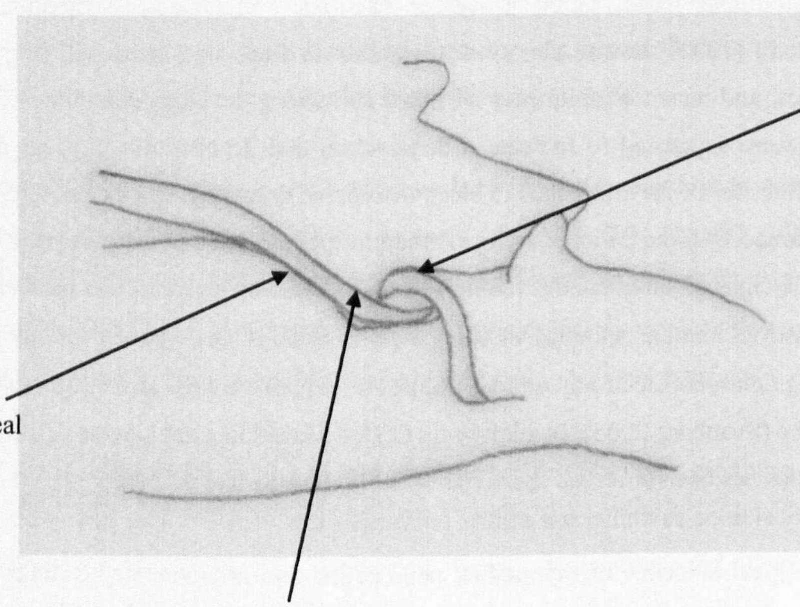
Histological abnormalities consistent with chronic denervation (fibre type grouping, mild atrophy, moth-eaten fibres and target fibres) were identified within the palatinus muscle in a confirmed DDSP afflicted horse and not in a control horse (Holcombe and Ducharme 2007). Histopathological evidence of palatal myositis was also suggested to occur in the free border of the soft palate in DDSP cases, however a definitive diagnosis of DDSP had not been achieved in these horses (Blythe *et al.* 1983). The histological findings of myonecrosis, phagocytosis and perimysial infiltration by macrophages and other mononuclear cells were reported to be representative of a low grade inflammatory myopathy. However similar changes were identified, although to a lesser degree, in control horses. It is unclear whether the increase in histological features of myositis were the cause or a consequence of DDSP.

Similar observations of the morphological and histological characteristics have been noted in the soft palate musculature in man. High coefficients of variation occur in human soft palate muscles and this was proposed to be normal morphological characteristic rather than evidence of a pathologic process (Stål and Lindman 2000). Although the histological appearance of the palatal musculature may differ from that of other muscles, several studies suggest a process of muscle denervation occurs in the palate muscles of OSA patients (Kimoff 2007; Svanborg 2005). Woodson *et al.* (1991) found atrophied and hypertrophied muscle fibres in the soft palate in patients with OSA and snoring but normal fibre size in non-snoring controls. Frequent focal degeneration of myelinated nerve fibres was also noted in severely apnoeic patients. Edstrom *et al.* (1992) showed fibre type grouping, grouped atrophy and great variability of muscle fibre size in the palatopharyngeus of OSA patients, these changes were not present in normal control subjects. They were considered typical of slowly progressive (chronic) motor neuron lesions, where denervation and reinnervation processes occurred simultaneously (Svanborg 2005). Lindman and Stahl (2002) showed abnormal variability in fibre size, increased proportions of small sized fibres, and increased frequency of fibres containing developmental MyHC isoforms. These findings were suggested to indicate a denervation and degeneration process and thus a neuromuscular disorder of the soft palate in sleep disordered breathing. The pathological findings were more pronounced in the palatopharyngeus than in the musculus uvulae. Boyd *et al.* (2004) also showed clear signs of simultaneous reinnervation (increase in intramuscular nerve fibres) and denervation (positive immunostaining) in soft palate muscle of OSA patients when compared with non snoring controls. Electromyography studies of palatal muscles also suggest progressive motor neuropathy (Svanborg 2005). In addition in OSA a transition from slow to fast fibres in the soft palate muscles has been observed (Series *et al.* 1996; Bradford *et al.* 2005).

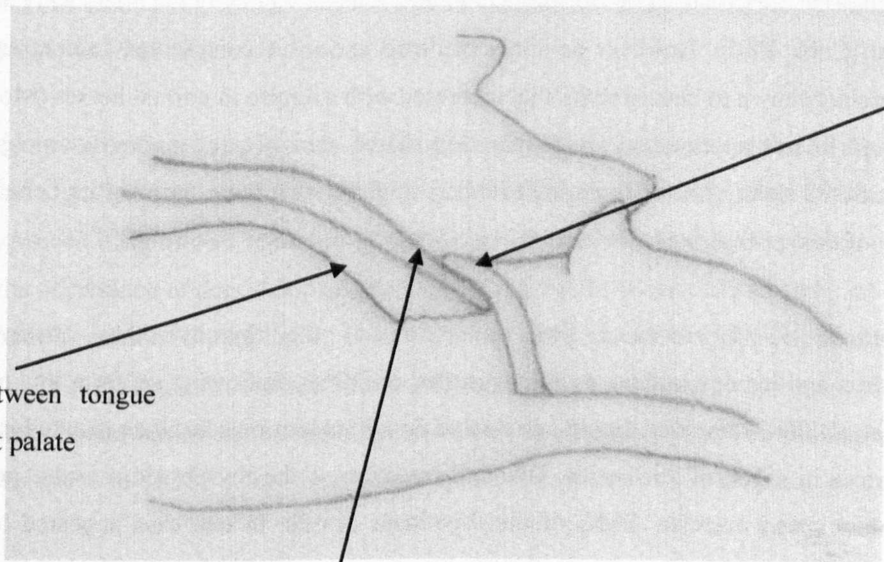
Although histological evidence of myopathic, neuropathic and inflammatory changes with soft palate muscles has been observed in OSA, it is also believed that many of these changes may occur secondarily (Eckert *et al.* 2007; Kimoff 2007; Series 2002; Svanborg 2005). Longstanding mechanical vibration and muscle stretch are known to cause nerve and muscle fibre damage (Stål *et al.* 2009).

3.4.1.3 Oropalatal seal

Ahern (1999a) proposed the existence of a functional seal between the ventral soft palate and the oropharyngeal mucosa which might be involved in maintenance of the normal soft palate position. In support of this hypothesis two contours of the caudal soft palate were described. In the first contour a concave trough in the caudal region of the soft palate was noted which was thought to suggest contact of the soft palate with the oropharyngeal mucosa (figure 3.6). The author suggested that this appearance could only be explained by the existence of an oropalatal seal (OPS), as intrinsic and extrinsic palatine muscular activity alone would be unlikely to produce and maintain this contour. In contrast the second contour described a convex appearance to the soft palate which was suggested to occur when air was able to enter the oropharynx causing failure of the OPS (figure 3.7). It was suggested that DDSP could only occur following disruption of the OPS.



3.6 Diagram of the nasopharynx, showing concave appearance to caudal soft palate and contact between ventral soft palate and the tongue



3.7 Diagram of the nasopharynx showing disruption of the oropalatal seal and close contact between the epiglottis and soft palate

Further research is required to confirm or refute whether air enters the oropharynx as a prequel of PI and/or DDSP, and whether it passes from the buccal cavity or from the nasopharynx. Opening of the mouth during exercise and caudal retraction of the tongue are thought to predispose to DDSP as a result of failure of the oropharyngeal seal (Cook 1981; Ahern 2005a).

3.4.2 Extrinsic factors

3.4.2.1 Laryngohyoid position

Laryngeal position was one of the earlier proposed mechanisms for palatal dysfunction and more recently hyoid position has been investigated. Cook (1981) proposed that excessive caudal retraction of the larynx would result in DDSP. Caudal retraction of the larynx prior to DDSP has subsequently been reported as a clinical scenario observed during treadmill endoscopy

(Ducharme 2006; Cheetham *et al.* 2009). It was originally suggested that caudal retraction would occur due to abnormally vigorous contraction of the strap muscles which might occur in a horse suffering from other respiratory disease, or may be the result of overreaction or spasm of the muscle in a normal horse caused by nervous excitement when a willing horse is suddenly asked to give its best (Cook 1981). However no study confirms excessive contraction. In contrast these muscles were not shown to have activity that increased with exercise in normal horses (Morello *et al.* 2008) and in an experimental study resection of the sternothyroideus and sternohyoideus muscles increased airway pressures during exercise, implying that these muscles are beneficial to the stability of the upper airway (Holcombe *et al.* 1994).

Tsukroff *et al.* (1998) revealed that transection of the thyrohyoideus, omohyoideus, sternohyoideus and hyoepiglotticus muscles resulted in DDSP. Following on from this research Ducharme *et al.* (2003) revealed that transection of thyrohyoideus muscle alone resulted in DDSP during exercise in seven of ten horses. Bilateral resection of the thyrohyoid muscles produced DDSP at slow speed exercise. EMG of the thyroideus muscle in one case appeared to show decreased activity immediately prior to DDSP (Ducharme *et al.* 2003). However, this has not been confirmed in a larger number of naturally occurring cases and there are no suggestions as to why specific dysfunction of this muscle may occur. The thyrohyoideus connects the hyoid and larynx, and it was suggested that the two move in unison (Tsukroff *et al.* 1998). Following resection of the thyrohyoideus muscle perhaps forces applied to one are not appropriately transmitted to the other.

It has been shown that the caudal hyoid muscles (omohyoideus, sternohyoideus, sternothyroideus, thyrohyoideus) had no further progressive increase in activity for increasing speeds therefore it was suggested that rostral displacement of the hyoid and larynx was the most important factor for airway stability (Morello *et al.* 2008). In other species rostral hyoid movement is achieved by activity of the genioglossus and geniohyoid muscles. In experimental horses, bilateral local anaesthetic blockade of the distal hypoglossal nerve induced DDSP during high speed exercise in 10 of the 19 experiments (Cheetham *et al.* 2009). It is unclear from this study exactly which muscles were affected by the nerve block, but it was proposed to be primarily the intrinsic and extrinsic tongue musculature. However, in two horses epiglottic retroversion also occurred and this was attributable to induced dysfunction of the hyoepiglotticus muscles. The authors suggested that the hypoglossal nerve block may induce DDSP by allowing caudal retraction of the hyoid apparatus or by preventing protrusion of the genioglossus muscle (Cheetham *et al.* 2009). However in equine cadavers and in anaesthetised horses it was shown that rostral protrusion of the tongue had no significant effect on hyoid position, whereas rostral traction of the geniohyoid did cause a significant cranioventral displacement of the basihyoid (Cornelisse *et al.* 2001b; Becker *et al.* 1999).

In a study investigating laryngohyoid position by ultrasound in horses with DDSP and those without, no significant associations with laryngeal position could be identified (Chalmers *et al.* 2009). However, a significant relationship was found between the depth of the basihyoid bone at rest and the occurrence of dorsal displacement of the soft palate at exercise, whereby on average a more ventral location of the basihyoid bone is present in horses with dorsal displacement of the soft palate. This finding is in contrast to the studies described earlier which suggest that ventral displacement of the basihyoid enlarges and stabilises the nasopharynx. The finding of a more ventral basihyoid in DDSP confirmed horses was not replicated in a different study (Garrett 2010).

It has been reported that patients with OSA have a more anterior and inferior position of the hyoid bone, associated with a lower position of the tongue (Vieira *et al.* 2011). Activity of the genioglossus and geniohyoid have been shown to be important in maintaining airway patency in humans and pathological changes in these muscles have been observed in OSA (Carrera *et al.* 1999). In addition, the genioglossus had a higher proportion of type II fibres and enhanced in vitro fatigability in OSA patients than controls (Carrera *et al.* 1999). Interestingly, the structural and functional changes in the genioglossus of OSA patients were reversed with the use of CPAP, also suggesting some of these changes are consequence rather than cause (Carrera *et al.* 1999).

3.4.2.2 Epiglottal factors

The relationship between the epiglottis and the soft palate is so tightly controlled that under normal circumstances horses are incapable of using the oral route for breathing i.e. they are obligate nasal breathers (Sisson and Grossman 1953). The epiglottis may assist in forming a seal which maintains the larynx within the nasopharynx thus preserving nasal breathing (Negus 1929). The position of the epiglottis is controlled by the position of the larynx and hyoid apparatus and by the hyoepiglotticus muscle (HE) (Van de Graaff *et al.* 1984).

Early reports suggested that the epiglottis functions as a rigid support to hold the soft palate in a ventral position (Cook 1981; Haynes 1981; Koch 1991; Tulleners 1995; Linford *et al.* 1983). Both epiglottic hypoplasia and epiglottic flaccidity have been proposed to cause palatal dysfunction. However, this is not well supported by more recent clinical or experimental studies. Poor associations between epiglottic size or conformation and DDSP during exercise have been found in high-speed treadmill studies (Kannegieter and Dore 1995; Rehder *et al.* 1995; Parente *et al.* 2002; Lane *et al.* 2006b). However, these may not be entirely appropriate comparisons as the epiglottis is assessed during resting endoscopy and compared with the soft palate position during exercise. Furthermore epiglottic length measured radiographically was considered normal in DDSP confirmed horses (Rehder *et al.* 1995; Courouce-Malblanc *et al.* 2010).

In experimental studies, a bilateral hypoglossal and glossopharyngeal nerve block caused epiglottic retroversion during inspiration at exercise (Holcombe *et al.* 1997b). However, despite complete loss of contact between the epiglottis and the soft palate, the soft palate remained in the normal position. The authors concluded that a functional epiglottis was not required to maintain soft palate stability (in horses with normal palate function). It has also been demonstrated that the hyoepiglotticus muscle has respiratory related EMG activity, predominately during inspiration (Holcombe *et al.* 2002). Furthermore, activity increased with increasing treadmill speed. Electrical stimulation of the hyoepiglotticus muscle produced ventral displacement of the epiglottis towards the soft palate and was thus thought to enlarge the aditus laryngis. In 3 of the 6 horses, conformational changes of the epiglottis occurred during electrical stimulation. The flattened epiglottic shape observed with the electrical stimulation appears similar to that described to occur during palatal instability (Lane *et al.* 2006a). Lane *et al.* (2006a) suggested that as the soft palate lifts in cases of PI and contacts the ventral surface of the epiglottis, further contraction of this muscle then occurs leading to the conformational change. Interestingly, although not described by the authors the images in the study by Holcombe *et al.* (2002) also show that the concave appearance of the caudal soft palate (as described by Ahern 1999a) appears to be lost during the electrical stimulation of the HE.

In other species the epiglottis has a role in oro-nasal partitioning. In rats, inspiratory activation of the HE muscle is thought to enhance the seal between the soft palate and epiglottis (Andrew 1954). Indeed a long standing concept of HE muscle function revolves around maintenance of a soft palate- epiglottic seal and the preservation of nasal route airflow (Negus 1929). However a more recent study showed that vigorous recruitment of this muscle in fact disrupts the seal between soft palate and epiglottis. Contraction of the HE muscle moves the epiglottis ventrally disengaging it from the soft palate. This opens the oral pathway for airflow by bringing the epiglottis to lie ventral to the soft palate. Thus, HE muscle recruitment promotes oral rather than nasal airflow (Amis *et al.* 1996b).

It is unclear whether a similar scenario might exist in horses during exercise i.e. a low level recruitment of HE is required to prevent ER, but vigorous recruitment leads to changes in epiglottic conformation seen with palatal dysfunction. It is unclear what factors promote more vigorous recruitment of this muscle.

3.4.2.3 Swallowing

Two studies have suggested that DDSP can occur immediately following a swallow (Parente *et al.* 2002; Rehder *et al.* 1995). However, a larger scale clinical study suggested this was in fact a rare occurrence (Lane *et al.* 2006a). It is unclear whether this difference might reflect breed differences. In the study by Rehder *et al.* (1995), 7 of 19 horses experienced DDSP associated with swallowing and 12 of the 19 horses were Standardbreds. In the study by Parente *et al.* (2002), 12 of 92 horses experienced DDSP associated with swallowing. When separated by breed it can be seen that 33% of SB displaced in association with swallowing whereas this occurred in only 8% of TB. The study by Lane *et al.* (2006a) was based entirely on TB and in only 1 of 237 horses did DDSP occur subsequent to deglutition. In the study by Rehder *et al.* (1995) horses had placement of a tracheal pressure transducer, this is likely to interfere with epiglottic movement during swallowing and therefore might have predisposed to DDSP.

An experimental study has shown that during exercise DDSP affected horses swallow significantly more frequently in the one minute preceding DDSP than do control horses (Pigott *et al.* 2010). This study also showed that in normal horses the frequency of swallowing decreases with increasing speed.

Lane *et al.* (2006a) suggested that deglutition appeared to be a corrective measure during palatal dysfunction to express air from the oropharynx and re-establish the oropharyngeal seal. Whereas others suggest that the swallowing manoeuvre corrects the caudal retraction of the larynx (Piggott *et al.* 2010). It was also proposed that decreased tongue muscle function during exercise leads to increased firing of tongue muscle proprioceptive fibres which triggers increased swallowing (Pigott *et al.* 2010). Another experimental study showed that electrical stimulation of the hyoepiglotticus muscle induced swallowing (Holcombe *et al.* 2002).

Although not studied repeated swallowing is likely to be detrimental to ventilation during exercise because respiration is suspended during deglutition.

3.4.2.4 Other

Lower airway disease has also been suggested to play a role in palatal dysfunction (Holcombe and Ducharme 2007). This has not been well studied and it is unclear whether a global respiratory tract infection occurs which affects the upper airway as described above or whether lower airway infections/ inflammation alters airflows or airway pressures which subsequently increases the likelihood of DDSP. Some studies have shown as association between DDSP and lower airway diseases (Courouce-Malblanc *et al.* 2010), whereas others have not (Franklin and Allen 2007). If there is an association it remains unclear whether this is cause or effect, as oral breathing following DDSP is thought to result in increased tracheal contamination.

Anecdotally it is suggested that musculoskeletal pain may cause DDSP in some horses (Courouce-Malblanc *et al.* 2010). The reasons for this have not been described and thus far have not been investigated.

3.5 Discussion

Currently the aetiopathogenesis of dynamic palatal dysfunction is not fully understood. There are numerous difficulties in studying the aetiopathogenesis of this condition which probably explains why further progress has not been made. Firstly studies need to compare a population of horses confirmed to have the condition against a population confirmed not to have the condition. As discussed in the previous chapter establishing a definitive diagnosis is difficult and costly to achieve and would require all horses entering training to reach a reasonable fitness level, prior to having treadmill endoscopy performed. Secondly, the muscles of the upper airway are difficult to access in order to biopsy in clinical cases and horses with this condition are rarely euthanased therefore post-mortem studies are also not possible.

It is possible that the causes are multifactorial for which DDSP is an end point. Researchers have attempted to establish the cause by searching for dysfunction in a specific muscle. In OSA it is known that the coordinated activity of many upper airway muscles is important for maintenance of pharyngeal patency. As yet a unifying concept has not been attempted which aims to draw several of the proposed mechanisms together.

Chapter 4 Critical review of the rationale for interventions for dynamic palatal dysfunction

Numerous interventions for dynamic palatal dysfunction have been described. It is important to understand the rationale and scientific evidence that lead to their development. This chapter discusses the mechanisms by which each intervention aims to address dynamic palatal dysfunction and the evidence to support this. The subsequent chapter investigates the reported efficacy of these interventions.

4.1 Soft palate procedures

Several surgical treatments have been described which aim to increase the tension or stiffness in the soft palate. As discussed in the previous chapter there is, at present, insufficient evidence to confirm whether or not increasing the stiffness improves palatal dysfunction. These methods do not address muscular strength of palatal musculature but aim to reduce the compliance of the soft palate through the induction of fibrosis (Ducharme 2006). The stiffening that results is thought to increase the intrinsic strength of the caudal soft palate so that it is able to resist the large pressure changes that occur within the nasopharynx during strenuous exercise.

A number of methods are described including thermal cautery of the oral surface (Ordidge 2001), laser cautery of the nasal surface (Gerstenberg and Dugdale 1998, Alkabes *et al.* 2010) or oral surface (Smith and Embertson 2005), an elliptical mucosal resection of the oral surface (Ahern 1993a) and palatal sclerotherapy (Cehak *et al.* 2006; Marcoux *et al.* 2008). For laser cautery, the use of a diode laser (Hogan *et al.* 2002, Alkabes *et al.* 2010), CO_2 laser (Smith and Embertson 2005) and Nd:YAG laser (Gerstenberg and Dugdale 1998) have been reported. For palatal sclerotherapy both sodium tetradecyl sulphate and poly-L-lactic acid have been used and are administered into the submucosa from the nasal aspect of the soft palate (Cehak *et al.* 2006, Marcoux *et al.* 2008).

A fibrous tissue reaction has been observed in response to injections of poly-L-lactic acid (Cehak *et al.* 2006) and diode laser (Alkabes *et al.* 2010), but not in response to low dose sodium tetradecyl sulphate injections (Munoz *et al.* 2010). The histopathological response to thermal cautery or mucosal resection has not been investigated. For tension palatoplasty by mucosal resection it has been presumed that the tension acquired increases with the width of the resection (Ahern 2005b). However it is known that suture dehiscence can occur (Ahern 2005b). In these cases it is presumed that secondary intention healing induces some degree of fibrosis. It is unclear whether mucosal resection and primary intention healing achieves greater increases in tension than mucosal resection and secondary intention healing.

Although laser palatoplasty of the nasal surface caused fibrosis, loss of soft palate skeletal muscle was also observed secondary to laser-induced thermal injury (Alkabes *et al.* 2010). Despite the development of fibrosis, the stiffness (or elastic modulus) actually decreased and the soft palates from treated horses were in fact more compliant than those of control horses (Alkabes *et al.* 2010). Franklin (2009) proposed that loss of muscle mass may well have been detrimental to soft palate stability. It is unclear whether the fibrosis failed to increase the palate stiffness or whether the loss of muscle mass despite the induction of fibrosis was responsible for the decrease in stiffness.

Staphylectomy is partial resection of the caudal border of the soft palate and was originally described as a treatment to address an excessively long soft palate. As discussed in the previous chapter there is insufficient evidence to support the assumption that a long soft palate is involved in the pathogenesis of dynamic palatal dysfunction. Staphylectomy has been performed by excision (Quinlan *et al.* 1949; Cook 1962) and more recently by laser (Onhesorge and Deegen 1998). The procedure is suggested to result in fibrosis and stiffening of the caudal border of the soft palate. The border of the soft palate showed increased thickness following laser staphylectomy due to extreme formation of connective tissue. However it also reduces the length of the soft palate thereby increasing the size of the intrapharyngeum ostium (Jager-Hauer *et al.* 2003). Rather than prevent displacement, this may reduce the degree of obstruction that occurs once displacement has taken place (Haynes 1983). O'Reilly *et al.* (1997) reported that staphylectomy (by excision) impairs upper airway mechanics in clinically normal horses. The staphylectomy procedure increased tracheal and translaryngeal inspiratory impedance significantly during exercise compared to pre-surgery (O'Reilly *et al.* 1997). Therefore the procedure appears to be detrimental when performed in normal horses; the affect on respiratory parameters in clinical cases of palatal dysfunction has not been studied.

Similar techniques of injection snoreplasty (IS), cautery-assisted palatal stiffening operation (CAPSO) and uvulopalatopharyngoplasty (UPPP) have been described in man. In man the aims are to stiffen and shorten the soft palate to prevent airway obstruction (Ellis *et al.* 1993). Uvulopalatopharyngoplasty is the longest standing of these procedures and involves removal of the uvula and caudal soft palate and therefore is similar to staphylectomy. UPPP was initially performed surgically but the technique was modified and is nowadays more commonly performed by laser (typically CO_2 laser). CAPSO is a method of burning the soft plate and is used as a means to remove a longitudinal strip of mucosa along the soft palate, with the resulting wound allowed to heal by secondary intention (Wassmuth *et al.* 2000). For IS several products have been injected including sodium tetradecyl sulphate, ethanol and polidocanol (Brietzke and Mair 2004, Poyrazoglu *et al.* 2006). In man these procedures are all performed from the oral surface.

Histological examination has revealed that both CAPSO and IS induce submucosal fibrosis and both procedures were considered to objectively stiffen the soft palate in a canine model (Lafrentz *et al.* 2003). The use of Nd:YAG laser on the oral surface of canine soft palates was also studied experimentally (Wang *et al.* 2002). The laser treatment caused shrinkage of the soft palate, which reduced the length. The thermal effects penetrated the full thickness of the mucosa and the submucosa but not the muscle. Laser tissue stiffening is suggested to occur in 2 phases. Firstly, an acute response resulting in mucosal shrinkage occurs which is considered a common phenomenon of laser tissue interactions. Subsequently there is a delayed response associated with tissue fibrosis, which is suggested to be the key step in laser stiffening. It is suggested to be produced by submucosal fibroblasts in a manner similar to wound healing (Wang *et al.* 2002). In contrast others have demonstrated detrimental long term effects of thermal injury to the human soft palate as a result of laser assisted uvulopalatoplasty (Berger *et al.* 1999). Pathological changes were observed in the epithelium, lamina propria and the central musculoglandular layer, which was considered to be far beyond the immediate range of the laser beam application. A dense fibrotic tissue reaction affected both the lamina propria and the musculoglandular layer. The massive fibrosis was reported to destroy the normal structure of the muscle bundles and it was suggested that the diminished contractility due to muscle loss would lead to a decreased upper airway calibre and eventually to further airway obstruction. Courey *et al.* (1999) studied porcine soft palates and confirmed that procedures that target the mucosa (electrocautery, CO_2 laser and radiofrequency) resulted in increased collagen deposition in the submucosa and increased tissue stiffness. Procedures in which the muscle is injured (primarily radiofrequency) result in increased collagen deposition and increased stiffness within the muscle. However, loss of muscle fibres was again observed and these authors also suggested that this had the potential to ultimately worsen airway obstruction through loss of muscle tone.

4.2 Procedures which alter laryngeal or laryngohyoid position

Interventions may alter laryngeal position by preventing caudal retraction of the larynx (tenectomy or myectomy of sternothyroideus, sternohyoideus and/ or omohyoideus muscles) (Harrison and Raker 1988; Duncan 1997) or by advancement of the larynx (laryngeal tie-forward procedure, laryngohyoid support device) (Ducharme *et al.* 2003, Woodie *et al.* 2005ab). As discussed there is incomplete evidence to support the assumption that caudal retraction of the larynx is the cause of DDSP.

The laryngeal tie-forward (LTF) procedure involves placement of a suture between the thyroid cartilage and the basihyoid bone, in an attempt to recreate the action of the thyrohyoideus muscle (Ducharme *et al.* 2003). Placement of the suture prevented DDSP in 5 of 6 thyrohyoideus-resected horses and was the basis for the development of the LTF procedure. The LTF has been confirmed by radiographs to move the basihyoid significantly dorsally and caudally and to move the larynx dorsally and rostrally at rest (Woodie *et al.* 2005a, Cheetham *et al.* 2008). The effect of sternothyroideus muscle resection on the position of the hyoid or larynx at rest has not been studied. Furthermore, due to imaging difficulties, no studies have been attempted to document the effect of either of these procedures on laryngohyoid position during exercise.

The LTF procedure did not have any significant affect on airway pressures in 10 normal horses (Ducharme *et al.* 2003). Whereas resection of the sternothyroideus and sternohyoideus muscles in normal horses increased pressures during exercise, implying that these muscles are involved in the stability of the upper airway (Holcombe *et al.* 1994). Translaryngeal and tracheal inspiratory pressures and translaryngeal and tracheal inspiratory resistances were significantly increased following muscle resection. It was proposed that these findings occurred due to altered upper airway geometry secondary to the loss of sternothyroideus and sternohyoideus muscle function

(Holcombe *et al.* 1994). The results of this study suggest this procedure has an adverse effect on upper airway mechanics in normal horses.

As discussed in the previous chapter, research from other species has suggested that the net effect of the combined actions of the rostral and caudal hyoid musculature is to cause ventral hyoid displacement thereby dilating the nasopharynx. It is unclear whether these procedures might be detrimental to this. Following sternothyroideus and sternohyoideus resection, there is likely to be less caudal force applied to the hyoid, which may subsequently effect the net ventral movement that is created. For the LTF one study has suggested that the procedure did inhibit the normal relationship of the larynx and hyoid (McCluskie *et al.* 2008). It appears that the LTF prevented the caudal movement of the larynx typically seen with head extension (McCluskie *et al.* 2008). It is unclear to what degree fixation of the larynx and hyoid relative to each other affects the normal function of the pharynx.

The hyoid advancement procedure has been described in man as a treatment for OSA. The procedure advances the hyoid complex in an anterior direction by placement of a suture to the mandible (Riley *et al.* 1989). A modification to the procedure was described (Riley *et al.* 1994) and although still called 'hyoid suspension' this is considered to be a misnomer and is more appropriately described as hyoidthyroidpexia (HTP) (de Vries and Verse 2010). With this procedure the hyoid is no longer fixated on the mandible but on the upper edge of the thyroid cartilage. HTP involves stabilizing the hyoid bone inferiorly and anteriorly by attaching to the superior border of the thyroid cartilage (den Herder *et al.* 2005) and is therefore a more similar procedure to LTF. It was suggested that the anterior movement of the hyoid improves the airway and reduces obstruction (den Herder *et al.* 2005), however the rationale of positioning the hyoid inferiorly is unclear when an inferiorly located hyoid has been suggested to be the cause of OSA in man.

4.3 Epiglottic procedures

It is proposed that epiglottic augmentation increases epiglottic size, thickness and rigidity thus helping to prevent DDSP during exercise (Tulleners *et al.* 1990). As previously discussed there is at present limited evidence to confirm the role of the epiglottis in dynamic palatal dysfunction. The use of autogenous or allogenous auricular cartilage grafts, bovine collagen and polytetrafluoroethylene ('polytef' or 'teflon') paste has been described in the horse (Tulleners and Hamir 1991). Polytef augmentation appears to be more effective in creating a uniform increase in epiglottic thickness than bovine collagen and auricular cartilage grafts (Tulleners and Hamir 1991). Tulleners and Hamir (1991) documented that injection of polytef resulted in a 40% increase in epiglottic thickness at the apex and a 29% increase in thickness at the region of attachment of the aryepiglottic folds. The procedure did not alter the length of the epiglottis. The epiglottic thickening created by the procedure was attributable to distension of the submucosal space with foreign body granulamata surrounded by fibrous connective tissue (Tulleners and Hamir 1991). Polytetrafluoroethylene was previously widely used to treat vocal cord paralysis in man (~Injection Laryngoplasty), however patients frequently developed serious long term complications such as 'Teflon granulomas' and this product has largely been excluded from modern laryngology in favour of other substances (Kwon and Buckmire 2004).

Resection of the sub-epiglottic mucosa has also been described and aims to prevent flaccidity of the epiglottis (Ahern 1993a). The mobility of this tissue was suggested to play a role in maintaining ventral positioning of the soft palate. However no studies have confirmed this or experimentally studied the effect of this surgery on the epiglottis.

4.4 Conservative procedures

Tack alterations such as nosebands and tongue ties have been advocated to prevent opening of the mouth and caudal retraction of the tongue which are thought to predispose to DDSP as a result of failure of the oropharyngeal seal (Cook 1981; Ahern 2005a). However the importance of the OPS has yet to be confirmed. Furthermore the effect of mouth opening on tongue and palate position has not been studied.

Cross or drop nosebands attempt to prevent opening of the mouth, whilst the Australian noseband holds the bit high in the horse's mouth reducing the likelihood of the horse getting the tongue over the bit (Dugdale and Greenwood 1993). The use of tongue bits with a caudal extension thought to exert pressure on the dorsal surface of tongue have also been described (Dugdale and Greenwood 1993). A bitless bridle has also been suggested as a treatment for DDSP, by reducing factors such as salivation and tongue withdrawal (Cook 2002). The tongue-tie aims to prevent caudal retraction of the tongue and was also thought to pull the hyoid apparatus and larynx forward (Dugdale and Greenwood 1993). However, application of a tongue tie did not improve airway dynamics in clinically normal horses during exercise (Beard *et al.* 2001; Cornelisse *et al.* 2001a) nor did it increase nasopharyngeal diameter or alter hyoid position in anaesthetised normal horses (Cornelisse *et al.* 2001b). Cornelisse *et al.* (2001b) suggested that depression of the root of the tongue rather than tongue protrusion may be important, but it is unlikely that this can be created with bits or tongue ties.

The laryngohyoid support device (LHS) ("cornell collar") also aims to reposition the larynx rostrally and dorsally (Woodie *et al.* 2005b) and has been described as a nonsurgical laryngeal tie forward (Barakzai and Hawkes 2010). The purpose of the device is to move the larynx dorsally by upward pressure on the ventral aspect of the thyroid cartilage and rostrally by applying forward pressure on the caudal aspect of the basihyoid bone. Radiographs obtained in 10 horses with and without the LHS confirmed that the larynx was moved dorsally and caudally (Woodie *et al.* 2005b). The effect of the LHS on the position of the basihyoid was not described, however if forward pressure is applied to the basihyoid it would be expected to be moved in a rostral direction. Thus the LTF and LHS appear to have the same effect on the larynx (i.e. rostral and dorsal) but different effects on the basihyoid, with the LTF moving the hyoid caudally and LHS moving the hyoid rostrally. The LHS had no significant effect on blood gases, airway pressures and air flows in normal horses during exercise and was confirmed to prevent DDSP in 7 thyrohyoideus resected horses (Woodie *et al.* 2005b).

4.5 Training, exercise and rest

It has been suggested that DDSP in young racehorses might improve with further training and increases in fitness (Dugdale and Greenwood 1993; Lane 1993; Barakzai and Dixon 2005; Ducharme 2008). If true it is unclear whether the pharyngeal dilator muscles directly respond to training or whether improvements in the locomotor muscles reduce the work of the respiratory system.

It is well known that locomotor muscles show responses to athletic training and it has been proposed in man that if a training stimulus were imposed upon the upper airway dilator muscles that it would be reasonable to expect these muscles to also show a response (How *et al.* 2007). It has been shown in rats that some upper airway muscles do show a response to endurance exercise and it was suggested that this exercise-mediated adaptation is related to the recruitment of these muscles as stabilisers of the upper airway during exercise (Vincent *et al.* 2002). The response of the upper airway muscles to training has not been studied in the horse. However, it has been shown that athletic training results in an increase in peak oxygen consumption in horses, without any change in peak minute ventilation (Art and Lekeux 1993). This results in a decreased ventilatory equivalent for O_2 which has also been observed in response to training in man (Art and Lekeux 1993). The decrease in the ventilatory equivalent means that trained horses breathe less air than do untrained horses to ensure a given oxygen consumption (Art and Lekeux 1993). It was suggested that this could imply that either the energy cost of ventilation is reduced, fatigue or the respiratory muscles is delayed or the reduction in O_2 uptake by the muscles is profitable to the locomotor muscles (Art and Lekeux 1993). It is as yet unclear to what degree these factors may play a role in addressing DDSP.

Exercise programs are also recommended in OSA but this is largely to cause weight loss rather than specifically to improve upper airway muscle strength or endurance.

A period of rest may be advised in conjunction with surgical interventions, medical interventions or as a sole intervention (Geiser 1983; Barakzai *et al.* 2009a). Geiser (1983) suggested that the period of rest should be a minimum of 4-6 months, however this recommendation appears to be empirical. Obviously resting a horse is in complete contrast to increasing the levels of exercise and there has been little published to explain the rationale for resting the horse. Presumably the time period might allow recovery from a potential inciting causes such as an URT infection. In OSA the use of CPAP results in an improvement in histological abnormalities of the soft palate, suggesting that these can occur as a consequence to OSA rather than the cause. During periods of rest with no high intensity exercise being performed, it is highly unlikely that DDSP would occur. Therefore if any histopathological changes had occurred as a consequence of repeated episodes of palate vibration during DDSP, the rest period may allow resolution. However, this hypothesis has not been studied.

4.6 Medical procedures

Medical treatments described are primarily the use of corticosteroids, which aims to minimise inflammation that may be causing primary palate dysfunction or dysfunction secondary to neuropraxia of the pharyngeal branches of the vagus (Holcombe *et al.* 1998; Parente *et al.* 2002; Ducharme 2003). However at present there is insufficient evidence to confirm the role of upper airway inflammation in clinical cases of palatal dysfunction.

Anti-inflammatories have also been advocated to treat enlarged lymphoid tissue in children with OSA (Kuhle and Urschitz 2011).

Table 4.1 Showing procedures for dynamic palatal dysfunction and their suggested mechanisms of action

Treatment category	Name of intervention procedure	Suggested aim of procedure
Soft palate	Thermal cautery	Increase palate stiffness
	Laser cautery	Increase palate stiffness
	Elliptical mucosal resection	Increase palate stiffness
	Palatal sclerotherapy	Increase palate stiffness
	Staphylectomy	Increase palate stiffness and shorten
Larynx and Hyoid	Tenectomy/myectomy of sternothyroid/ sternohyoid/omohyoid	Prevent caudal retraction of the larynx
	Laryngeal tie-forward	Advance larynx
	Laryngohyoid support device	Advance larynx
Epiglottis	Epiglottic augmentation Subepiglottic resection	Increase thickness and rigidity Prevent epiglottic flaccidity
Conservative	Noseband	Prevent mouth opening
	Tongue tie	Prevent tongue retraction
	Bitless bridle	Prevent mouth opening/swallowing
	Rest	Allow resolution of underlying pathology
	Fitness	Improve muscle tone
Medical	Corticosteroids	Address inflammation

4.7 Discussion

Many interventions for dynamic palatal dysfunction have been developed to address the many proposed mechanisms. The poor understanding of the aetiopathogenesis has impacted on the evidence available to support the development of these interventions. Many of the interventions were used clinically without any experimental studies first being performed.

Several of the treatments described have strong similarities to treatments developed to address snoring or OSA in man. However, for a few of these procedures the oral approach is easier in man, where as a nasal approach using transendoscopic equipment is easier in horses. However the palatinus and palatopharyngeus muscles are located immediately below the nasal mucosa. The thick glandular layer is located on the oral side of the musculature. There is some evidence to suggest that palatoplasty procedures performed on the nasal side may cause loss of muscle fibres which may prove detrimental to upper airway stability. Procedures performed on the oral side may prove safer as fibrosis of the oral mucosa, sub mucosa or glandular layer could be created without damage to the more dorsal muscular layer. The effect of LTF on laryngohyoid position has been well studied. If evidence was available that better confirmed the involvement of laryngeal position in the pathogenesis of DDSP, the rationale for this treatment would be better supported. The long term side effects of polytetrafluoroethylene use in man are concerning and if research into epiglottic augmentation as a treatment continues the use of alternative substances should be investigated. There is little evidence to support the rationale for the use of the tongue tie and other conservative measures have received no experimental study. The use of corticosteroids would be considered appropriate if evidence was available to confirm the role of inflammation in palatal dysfunction.

In conclusion, due to the poor understanding of the aetiopathogenesis and the paucity of well designed studies for many advocated procedures there is insufficient evidence to confirm the rationale for their use. The subsequent chapter investigates the reported efficacy of these interventions in clinical cases.

Chapter 5 A systematic review of the efficacy of interventions for dynamic intermittent dorsal displacement of the soft palate

5.1 Introduction

Often decisions for interventions are made based upon the most recent or well-known study or upon expert opinion (Sheldon 2005). A systematic review is a process of combining information from all relevant studies to understand the knowledge base better, aiming to improve the reliability and accuracy of recommendations when compared to single studies. Systematic reviews are particularly useful when there are variations in clinical practice and when there is uncertainty over potential benefits and harms of an intervention. Studies may be combined in two ways: meta-analysis is the statistical synthesis of results of similar studies into a single quantitative estimate of effect (Haynes 2006b), whilst narrative synthesis is the process of synthesising primary studies to explore heterogeneity descriptively rather than statistically (Popay *et al.* 2006).

As previously described the aetiopathogenesis of DDSP remains unclear and numerous treatment options have been developed in order to address the different proposed mechanisms. It was noted that for many interventions there is limited scientific evidence to confirm the rationale for their use. Therefore the efficacy of treatments for palatal dysfunction remains controversial and there is little consensus about how best to treat this condition.

5.2 Objectives

The aims of this paper were to systematically review the literature to assess the evidence on the efficacy and harms of interventions for dynamic intermittent DDSP and to assess whether factors relating to study quality affected the reported success rates.

5.3 Inclusion criteria for studies in this review

Types of studies: Studies of level 4 evidence and above (http://www.cebm.net/index.aspx?o=1025) were included. Where comparator groups were studied these included interventions that were compared with each other, or with affected horses that underwent no intervention or a comparison population without the condition.

Participants: Adult horses in which naturally occurring dynamic intermittent DDSP was diagnosed (as defined in the primary source reports) were included. Foals, cases with persistent DDSP, experimentally-induced DDSP and horses undergoing concurrent interventions for other URT conditions were excluded.

Interventions: Surgical interventions: Individual and combination surgical procedures were included. Studies were excluded when the results of different surgical procedures or different combinations of surgical procedures were presented as one result and it was not possible to determine which success rates were related to which intervention. However, for several procedures slight variations in the individual surgical techniques were permitted. For myectomy/ tenectomy, variation in muscle group and method of resection was allowed. For tension palatoplasty, concurrent subepiglottal resection was allowed and for the laryngeal tie-forward procedure, concurrent sternothyroid tenectomy was allowed.

Conservative and medical interventions: Individual and combination conservative interventions were included. Studies were permitted when the results of different conservative procedures were presented as one result.

Outcome measures: The success of the intervention (in the primary source reports) included either subjective or objective outcome measures. Subjective measures include assessment by the owner/ trainer of decreased respiratory noise or increased performance. Objective outcome measures include the analysis of race form pre and post intervention and pre post intervention treadmill endoscopic examination. All adverse effects of the intervention reported in the trial were included.

Publication: Publications from 1990 onwards, with English language text copy were considered.

5.4 Search methods

Studies were identified from electronic databases including MEDLINE, PUBMED, ISI Web of Science, CAB abstracts, EMBASE and IVIS (for conference proceedings) in October 2008 and repeated in November 2009. The search term used was (horse OR equine) AND (dorsal displacement of the soft palate OR soft palate) AND (treatment). Bibliographies of referenced textbooks and the reference lists of all retrieved studies were hand-searched for additional relevant studies. 18 authors/ centres were contacted to identify unpublished and ongoing studies.

All retrieved bibliographic references were managed in EndNote X reference manager software[2]. The abstracts and titles of references retrieved were screened for relevance. Full paper copies of potentially relevant articles were assessed for inclusion by two independent reviewers.

5.5 *Methods of the review*

5.5.1 Assessment of study quality

Study quality was assessed according to pre-established criteria (Appendix I). The basis of this quality assessment checklist was formed in a pilot phase using guidelines from the Centre for Reviews and Dissemination (www.york.ac/inst/crd/) and the Cochrane Collaboration Handbook (www.cochrane.org/resources/handbook), and consensus statements from STROBE (Strengthening the reporting of observational studies in epidemiology) (www.strobe-statement.org), MOOSE (meta-analysis of observational studies in epidemiology) (www.consort-statement.org) and CONSORT (www.consort-statement.org); and quality assessment checklists used in systematic reviews of snoring and obstructive sleep apnoea (Main *et al.* 2009). In addition, criteria were added that were thought to be particularly relevant to the field of equine dynamic upper respiratory tract interventions.

5.5.2 Data extraction, statistical analysis and data synthesis

Data for each study and relevant results are presented in summary tables (Appendix II). The effect measures reported by the trial authors were used. Where possible a quantitative analysis was performed and effectiveness summarised as odds ratio using 95% confidence intervals. The statistical analysis was performed using Review Manager software[1] using the Mantel-Haenszel method for dichotomous data.

Due to variations in study design, diagnostic method, comparator and outcome measure for each intervention a meta-analysis was not applicable. Therefore results were combined using a narrative synthesis (Popay *et al.* 2006). Differences between studies assessing the same intervention were explored narratively by examining differences in the study design and quality, diagnostic method and outcome measure.

5.6 *Results*

5.6.1 Quantity and quality of the research available.

The combined searches identified 1193 studies, of which 1117 were excluded based on the title. Seventy six were assessed and 23 studies were included (table 5.1). The bibliographic details of excluded studies and reasons for exclusion are detailed (Appendix III).

The evidence base covers a wide number of interventions, but differs widely in terms of study design, sample size, method of diagnosis, outcome measure and the number of cases lost to follow-up. There was an overall preponderance of studies towards surgical interventions.

Nine studies were case series and two were case reports, in which no comparator group was included. Five studies were described as case-control studies, however, insufficient information about the comparator population was provided so the appropriateness of the comparisons could not be fully assessed. In particular, where control horses were randomly selected, their DDSP status was unknown. Seven studies compared two surgical interventions, however only 3 assessed this statistically.

Only 3 studies (plus the two case reports) were based on horses in which a definitive diagnosis of DDSP was made in all included horses. In a further two studies a definitive diagnosis of palatal dysfunction (PI or DDSP) was achieved in all horses.

Three studies determined efficacy of the procedure using subjective outcome measures, fourteen used race performance and three reported both subjective and race performance outcomes. Only two studies and the two case reports used exercising endoscopy as an outcome measure. One of these studies also used subjective measures. The sample sizes varied from 1 to 405 at the intervention stage and from 1 to 197 at the analysis stage. In no study was a sample size calculation performed. In many studies a large number of horses underwent the procedure and were not included in the efficacy analysis. Some studies failed to report how many horses underwent the procedure but did not meet the inclusion criteria for analysis. For the 16 studies in which this information was available, 11 studies had less than 80% of horses in the analysis.

Assessment of adverse effects was severely limited because of lack of reporting. It was frequently unclear whether no adverse events occurred or whether adverse events were not reported.

Table 5.1 The methodological features of included studies

Study reference	Sample size at intervention stage	Sample size at analysis stage	What percentage of horses included in this review had a definitive diagnosis?	Outcome measure used	Were adverse effects reported?
Ahern (1993b)	111	100 * of which 95 included in this review+.	0	Subjective	No
Anderson *et al.* (1995)	209	149	0	Objective-race data Subjective	No
Barakzai *et al.* (2004)	104	53	0	Objective-race data	No
Barakzai and Dixon (2005)	unclear	31	23% DDSP (+ 6% PI)	Objective-race data	No
Barakzai *et al.* (2009a)	unclear	78	100% DDSP	Objective-race data	Yes
Bonenclark *et al.* (1999)	87	44	Unclear	Objective- race data	No
Cheetham *et al.* (2008)	263	106	34% DDSP (+ 12% PI)	Objective-race data	No
Dart (2006)	n/a	1	100% DDSP	Objective-treadmill endoscopy	Yes
Duncan (1997)	unclear	50	0	Objective-race data	Yes
Dykgraaf *et al.* (2005)	96	77* of which 58 included in this review+	Unclear	Objective-race data	No
Franklin et al. (2002b)	6	6*	100% DDSP	Objective-treadmill endoscopy	No
Franklin *et al.* (2009a)	234	197*	61% DDSP (+ 39% PI)	Objective– race data	No
Llewellyn and Petrowitz (1997)	405	41	0	Objective-race data	Yes

Marcoux *et al.* (2008)	8	8*	0	Subjective	Yes
McCluskie *et al.* (2009)	116	42, of which 29 included in this review+	72% DDSP (+ 28% PI)	Objective- treadmill endoscopy Subjective	No
Ordidge (2001)	252	187	0	Subjective	Yes
Parente *et al.* (2002)	92	32	100% DDSP	Objective- race data	No
Peloso *et al.* (1992)	1	1	100% DDSP	Objective- treadmill endoscopy	Yes
Picandet *et al.* (2005)	unclear	51	0	Objective- race data Subjective	Yes
Reardon *et al.* (2008a)	unclear	110	0	Objective- race data	Yes
Reardon *et al.* (2008b)	98	35	0	Objective- race data	No
Smith and Embertson (2005)	102	73	Unclear	Objective- race data	Yes
Woodie *et al.* (2005a)	116	98, of which 20 included in this review+	100% DDSP	Objective-race data Subjective	Yes

Key: DDSP dorsal displacement of the soft palate, PI palatal instability, *indicates that ≥80% of horses that underwent procedure were included in analysis, + horses that underwent concurrent surgeries for other URT obstructions were removed from this review.

5.6.2 Intervention summaries

Below is a summary of the evidence to support each of the included interventions. The heterogeneity of studies means that results are often not directly comparable. It is therefore difficult from the current evidence to draw firm conclusions regarding the true efficacy of these procedures or to determine which procedures might be the most successful and least harmful for treatment of DDSP.

5.6.2.1 Oral palatopharyngoplasty (Ahern procedure)

One study was identified which assessed this procedure (elliptical oral palatine mucosal resection and subepiglottic mucosal resection) (Ahern 1993b). The results of 95 horses were included in this review. The level of evidence provided by this study is low. A definitive diagnosis was not achieved. The outcome measure is largely subjective, not clearly defined and varies between horses. Although the reported results (74% success rate) suggest efficacy of the treatment, further evidence is needed to support this.

5.6.2.2 Oral palatoplasty by thermal cautery

This review identified five studies investigating the efficacy of thermal cautery (Ordidge 2001; Barakzai *et al.* 2009a; Reardon *et al.* 2008a; Franklin *et al.* 2009a; McCluskie *et al.* 2009). Variation in the surgical technique to include sub-epiglottic resection in some horses was reported by Franklin *et al.* (2009a) and McCluskie *et al.* (2009), however this had no effect on the reported efficacy of the procedure (Franklin *et al.* 2009a). Three studies assessed more than 100 cases: Ordidge (2001) n=187, Reardon *et al.* (2008a) n=110, Franklin *et al.* (2009a) n=103); a further study assessed 48 cases (Barakzai *et al.* 2009a) and the final study assessed only 12 cases (McCluskie *et al.* 2009). A definitive diagnosis of palatal dysfunction was obtained in all horses in three of the studies (Barakzai *et al.* 2009a; Franklin *et al.* 2009a; McCluskie *et al.* 2009). These studies used appropriate comparator groups of alternative interventions for DDSP (Barakzai *et al.* 2009a; Franklin *et al.* 2009a; McCluskie *et al.* 2009) and one study assessed the treatment group against a comparison population (Reardon *et al.* 2008a).

The outcome measures varied widely between studies. The pre post study (Ordidge 2001) provides the weakest level of evidence because no comparator group was included, subjective assessment was used and horses did not have a definitive diagnosis. The initial results from this study reported a high number of trainers (72%) considered this treatment to be successful.

However, only 48% of the horses that were reported to make 'gurgling' noise pre surgery ceased 'gurgling' after surgery. One study reassessed horses by endoscopic examination on a high-speed treadmill (McCluskie *et al.* 2009). The results showed that for 6 horses with DDSP, 3 still had DDSP and 3 improved from DDSP pre-intervention to palatal instability following the intervention. Of six horses initially diagnosed with PI, 5 continued to have PI post surgery and 1 had progressed to DDSP. However, a large proportion of horses in this study (68%) failed to have a repeat endoscopic examination and therefore the results may be biased, potentially towards the least successful cases. Three studies used race form as the outcome measure (Barakzai *et al.* 2009a; Reardon *et al.* 2008a; Franklin *et al.* 2009a). There is considerable variation in the number of races (1-5) that were assessed pre and post intervention, and variation in whether earnings, ratings or a performance index was used. The reported improvement in race performance varied depending on which race parameter was assessed: 28-51% (Reardon *et al.* 2008a), 32-59% (Franklin *et al.* 2009a) and 35-40% (Barakzai *et al.* 2009a).

When thermal cautery was compared with conservative interventions one method of measuring outcome favoured conservative treatment, however several other outcome measures revealed no significant difference between the groups (Barakzai *et al.* 2009a). No significant differences were found when thermal cautery was compared with laryngeal tie-forward or laryngeal tie-forward in combination with thermal cautery. However, there was a trend towards cautery being more successful than laryngeal tie-forward alone and the combination procedure being more successful than cautery alone (Franklin *et al.* 2009a). In another study there was no significant effect of cautery on the change in race parameters between cautery and comparison groups for 3 races pre and post. There was a significant effect on performance index for 1 race v 1 race and 1 race v 3 races; however this was not thought to be clinically relevant because of the large percentage of horses that showed no change (Reardon *et al.* 2008a). Treated horses had significantly lower race parameters in the last race before surgery than comparison horses although a direct comparison of the races after was not provided (Reardon *et al.* 2008a).

Three studies reported the prevalence of adverse effects and intra and post operative complications were not identified in two studies (Barakzai *et al.* 2009a; Reardon *et al.* 2008a). Possible discomfort for up to 36 hours was reported by Ordidge (2001) but details on the number of horses affected were not provided.

In conclusion, although the earlier study by Ordidge (2001) reported a high success rate (72%) this has not been verified by subsequent, better quality studies. The majority of studies performed to date suggest that this surgery is likely to result in only modest success (28 - 59%).

5.6.2.3 Laryngeal tie-forward procedure

Four studies assessing the efficacy of laryngeal tie-forward (LTF) as the sole procedure were included: Woodie *et al.* (2005a), Cheetham *et al.* (2008), Franklin *et al.* (2009a) and McCluskie *et al.* (2009). In addition, a single case report, documenting potential adverse effects was also included (Dart 2006). Variations to the surgical technique have been reported, with some horses undergoing a concurrent sternothyroid tenectomy. Cheetham *et al.* (2008) showed no significant difference between the original and modified technique on any measure of laryngohyoid movement and Franklin *et al.* (2009a) found no significant differences in success rates with the variations in surgical technique.

Woodie *et al.* (2005a) reported the success rate for 98 horses, however the results of only 30 could be included in this review because these were reported separately and it was not possible to determine from the manuscript which of the other 68 horses had undergone additional surgeries of the URT. All 30 horses had a definitive diagnosis of DDSP. Of these 30 horses, 20 (67%) were assessed using race performance and 80% were reported to have increased earnings and performance index following the procedure. A second study used race performance to assess 106 horses, of which 46% had a definitive diagnosis of palatal dysfunction (Cheetham *et al.* 2008). The results suggested that the procedure restored race earnings to baseline values (i.e. those prior to identification of DDSP) and that of the comparison population, but it is unclear in what proportion of horses this occurred (Cheetham *et al.* 2008). Only 66% of definitively diagnosed horses raced post operatively, therefore the proportion that show an improved measure of race performance is likely to be substantially lower than 66% and substantially lower than the 80% reported by Woodie *et al.* (2005a). Cheetham *et al.* (2008) found that horses that raced pre surgery were more likely to race post surgery, suggesting that when the inclusion criteria was restricted to only include horses that had raced 3 times pre-operatively (Woodie *et al.* 2005a) that this may have biased the results toward the more successful cases. Another study of 31 horses with palatal dysfunction revealed that the success rate of LTF alone varied from 26 - 62% depending on how race performance was assessed (Franklin *et al.* 2009a). When LTF was compared with thermal cautery or LTF in combination with thermal cautery, one method of measuring outcome identified that LTF alone was significantly less successful than when performed in combination with cautery, however another method found no significant difference between the groups (Franklin *et al.* 2009a). In the final study, efficacy of LTF was assessed by treadmill endoscopy before and after the procedure but only a small number of horses were assessed (McCluskie *et al.* 2009). Seven of 8 horses still experienced DDSP following the procedure; however there was potential bias in this study towards less successful cases.

One case report of adverse effects was identified, and the authors suggested that bilateral vocal fold collapse may have occurred subsequent to the LTF procedure (Dart 2006). In addition, this horse still experienced DDSP after the procedure. Complications of the procedure were also reported in 7% of the original 116 horses described by Woodie *et al.* (2005a) and 6% of improved horses were reported to have recurrence of DDSP.

Although the first study by Woodie *et al.* (2005a) suggested good efficacy of the procedure, subsequent studies have reported lower success rates that were not different from those reported for other procedures. Although attempts have been made to have better quality studies, the wide variation in results (13 – 80%) means that it is not possible to accurately determine the true efficacy of this procedure from the current evidence available and further studies are therefore recommended. In addition, further understanding of the role of laryngohyoid position is required. Cheetham *et al.* (2008) found that whilst horses with a more dorsal post operative position of the basihyoid and thyroid were more likely to race post operatively, horses with a more rostral post operative laryngeal position were less likely to race post operatively, questioning the rationale for the laryngeal tie-forward.

5.6.2.4 Composite surgery - combination of laryngeal tie-forward and thermal cautery

Three studies were identified investigating the effect of laryngeal tie-forward and thermal cautery in combination (Reardon *et al.* 2008b; Franklin *et al.* 2009a; McCluskie *et al.* 2009). Franklin *et al.* (2009a) assessed 63 horses, Reardon *et al.* (2008b) 43 horses and McCluskie *et al.* (2009) 9 horses. A definitive diagnosis of palatal dysfunction was achieved in 2 of the studies (Franklin *et al.* 2009a; McCluskie *et al.* 2009).

Two studies compared the results to either procedure performed alone (Franklin *et al.* 2009a; McCluskie *et al.* 2009) and one study to a comparison population (Reardon *et al.* 2008b). In the study where repeat treadmill endoscopy was performed (McCluskie *et al.* 2009), 3 of 7 horses still had DDSP and 4 had PI post operatively. Also 2 horses in which only PI was diagnosed initially were unchanged post operatively. As discussed previously this study had the potential for bias. Both studies assessing race performance found a wide variation in success rate depending on the outcome measure used: Reardon *et al.* (2008b) reported success rates of 42-67% and Franklin *et al.* (2009a) reported success rates of 38-73%. When the combination surgery was compared with either procedure performed alone, one method of measuring outcome favoured the combination procedure however another method found no significant difference between the groups (Franklin *et al.* 2009a). Reardon *et al.* (2008b) reported that a combination of LTF and thermal cautery resulted in a significant improvement in earnings, Racing Post ratings and performance index when 1 race pre v 1 race post surgery was assessed. When compared with the comparison horses, cases had a significant decrease in earnings, Racing Post ratings and performance index in the last race before surgery and post surgery these parameters were returned to baseline values and that of the comparison horses. However, when 3 races pre and post surgery were compared no significant difference between cases and comparison horses were found. A large proportion of the original population was lost from the analysis in this study and this may have biased results. The adverse effects were not reported in any study.

Again, there is wide variation (38-73%) in reported results and further evidence is required to confirm whether this combination of procedures is more effective than either procedure alone.

5.6.2.5 Staphylectomy

Only one study assessing staphylectomy (by excision) as a sole procedure was identified. This assessed the procedure in 69 horses and the success rate was compared to sternothyroideus myectomy (Anderson *et al.* 1995). A definitive diagnosis of DDSP was not achieved. The adverse effects of this procedure were not studied. The results based on race earnings (59% successful) were similar to those for sternothyrohyoideus myectomy. The level of evidence provided by this single study is low and further evidence is needed to support this treatment.

5.6.2.6 Myectomy/ tenectomy of sternothyrohyoideus/ omohyoideus

Five studies were identified; one case report (Peloso *et al.* 1992), two case series (Duncan 1997; Bonenclark *et al.* 1999) and two parallel group studies (Anderson *et al.* 1995; Parente *et al.* 2002). There is variability in the surgical procedure depending on the study. In three studies sternothyrohyoideus myectomy was performed (Peloso *et al.* 1992; Anderson *et al.* 1995; Parente *et al.* 2002), in one study sternothyroideus, sternohyoideus and omohyoideus myectomy was performed (Duncan 1997) and in one sternothyroideus tenectomy was performed (Bonenclark *et al.* 1999). The case report used treadmill endoscopy on 3 occasions pre and post surgery to determine the efficacy of the procedure. DDSP was observed in all 3 occasions pre-operatively and all 3 occasions post-operatively and therefore was deemed ineffective in this horse (Peloso *et al.* 1992). The number of horses assessed in the other studies was 80 (Anderson *et al.* 1995), 50 (Duncan 1997), 30 (Bonenclark *et al.* 1999) and 7 (Parente *et al.* 2002). In only one of these was a definitive diagnosis achieved (Parente *et al.* 2002). Success was assessed objectively using race performance and the reported success rates were from 50-70% (Anderson *et al.* 1995; Duncan 1997; Bonenclark *et al.* 1999; Parente *et al.* 2002). Adverse effects were only reported in one study, and were considered minor (Duncan 1997). Although the reported results suggest some efficacy of the treatment, the majority of studies performed to date have been of low quality. Further evidence is required to support these findings.

5.6.2.7 Composite surgery - combination surgery including sternothyroideus myotomy/ tenectomy and staphylectomy

Six studies were identified which describe the results of varying combination surgeries. Three studies assessed sternothyroid tenectomy and staphylectomy (Bonenclark *et al.* 1999; Parente *et al.* 2002; Dykgraaf *et al.* 2005), sternothyroid tenectomy, staphylectomy and thermoplasty was also assessed by Dykgraaf *et al.* (2005), sternothyroideus myotomy and staphylectomy was assessed by Llewellyn and Petrowitz (1997), sternothyroideus myotomy, staphylectomy and photothermoplasty by Smith and Embertson (2005) and sternothyrohyoideus myectomy, staphylectomy and ventriculectomy by Barakzai *et al.* (2004). The numbers of included cases were 11 (Parente *et al.* 2002), 18 (Bonenclark *et al.* 1999), 41 (Llewellyn and Petrowitz 1997), 53 (Barakzai *et al.* 2004) and 73 (Smith and Embertson 2005). Dykgraaf *et al.* (2005) assessed one group of 9 cases and one group of 49 cases. Two studies present the results of the combination surgeries without comparison groups (Llewellyn and Petrowitz 1997; Smith and Embertson

2005). In five of the six studies a definitive diagnosis was not achieved (Llewellyn and Petrowitz 1997; Bonenclark *et al.* 1999; Barakzai *et al.* 2004; Dykgraaf *et al.* 2005; Smith and Embertson 2005). Overall success rates from 60-78% were reported.

One study found a significant effect of surgery when compared with a comparison population (Barakzai *et al.* 2004). Although the main limitations of this study were the absence of a definitive diagnosis and the fact that 49% of cases were lost to the study because it was not possible to match to comparison horses. In 2 studies the reported success rate were higher for sternothyroid tenectomy and staphylectomy combined compared with either sternothyroid tenectomy or sternothyroideus myectomy alone, however statistical differences could not be confirmed (Bonenclark *et al.* 1999; Parente *et al.* 2002). There were no significant differences in the success rates between sternothyroid tenectomy and staphylectomy versus sternothyroid tenectomy, staphylectomy and thermoplasty (Dykraaf *et al.* 2005).

In four studies adverse effects were not reported (Bonenclark *et al.* 1999; Parente *et al.* 2002; Barakzai *et al.* 2004; Dykgraaf *et al.* 2005) and in one study no complications were observed in any horse (Smith and Embertson 2005). Llewellyn and Petrowitz (1997) reported haemorrhage, exuberant palatine granulation tissue, postoperative swelling and redevelopment of DDSP; however the numbers experiencing these complications were not listed.

Whilst the studies examined revealed moderate success rates, these studies are generally of low quality and it remains unclear whether combination surgeries are more beneficial than the individual procedures.

5.6.2.8 Palatal Sclerotherapy

Two studies were identified (Picandet *et al.* 2005; Marcoux *et al.* 2008), which assessed 51 and 8 horses respectively. A definitive diagnosis was not achieved in either study. In the study by Marcoux *et al.* (2008) 7 horses had some improvement in abnormal noise, although 7 of the 8 needed a second treatment. In the other study 60% ceased making abnormal noise and 70% had some improvement in race times. No major side effects were reported in either study, although minor side effects were described in 3 of 8 horses in the study by Marcoux *et al.* (2008). Although the reported results suggest possible efficacy of the treatment, the low quality of these studies means that further evidence is needed to support this.

5.6.2.9 Epiglottic augmentation

One case report (Peloso *et al.* 1992) and one case series (n=8) (Parente *et al.* 2002) investigating epiglottic augmentation alone were identified. In both studies, all horses had a definitive diagnosis of DDSP. The case report monitored the effects of epiglottic augmentation by repeat resting and treadmill endoscopy. The reported complications of reddened and oedematous epiglottis and coughing persisted for 3 weeks after surgery (Peloso *et al.* 1992). DDSP did not occur during 3 treadmill tests post operatively and the treatment was considered successful. However, it is unclear whether the horse performed at the same speed/ distance during the treadmill exercise test as previously. In the case series, eight horses underwent epiglottic augmentation and 50% were reported to improve earnings per start. Because of the limited number of cases studied to date, further evidence is required to support this treatment. However, the duration of side effects of the procedure should be considered and evaluated if future studies are undertaken.

5.6.2.10 Medical

Only one study assessing the effects of oral corticosteroids in combination with rest in six horses was identified (Parente *et al.* 2002). All horses had a definitive diagnosis of DDSP. Outcome was assessed using race performance and treatment was reported to be effective in 100% of cases. However, no details on the drug administered, dosage regime and course of medication was provided. The results suggest efficacy of the treatment, however the study included few horses and further studies are needed to provide additional evidence to support this.

5.6.2.11 Conservative

Three studies were identified assessing the efficacy of conservative treatments. One case series assessing the efficacy of the tongue tie alone was identified (Franklin *et al.* 2002b). In this study six horses previously diagnosed with DDSP during treadmill endoscopy underwent a second treadmill endoscopy test with a tongue tie in place. In 2 horses DDSP did not occur with a tongue tie in place; however PI was still observed (Franklin *et al.* 2002b). In 3 of the remaining 4 horses DDSP occurred earlier in the exercise test with the tongue tie on, although the differences were not statistically significant.

The other two studies assessed a range of conservative measures (drop noseband, tongue tie, rest, increased fitness) (Barakzai and Dixon 2005; Barakzai *et al.* 2009a). One study compared the efficacy of conservative measures in 31 horses against a comparison population (Barakzai and Dixon 2005) and the other study compared conservative measures in 30 horses against a group undergoing thermal cautery (Barakzai *et al.* 2009a). In the first study 29% of horses had a definitive diagnosis and in the second study all horses had a definitive diagnosis. These 2 studies reported conservative measures to be successful in 53-63% of horses. There was a significant increase in earnings in the conservative group but not for the comparison group. The proportion of conservatively treated horses that improved was also higher than for comparison horses but this was not significant (Barakzai and Dixon 2005). When compared with thermal cautery one method of measuring outcome favoured conservative treatment, however several other outcome measures revealed no significant difference between the groups (Barakzai *et al.* 2009a).

The evidence to support conservative measures in these studies is weakened by the fact that although conservative measures were advised to the trainer, there was no information reported on what was actually undertaken by the trainer. In addition, as many conservative measures were analysed together it is unclear which treatments or combinations of treatments may be effective.

No studies were identified investigating the 'cornell collar' in naturally occurring DDSP or anecdotally advocated treatments such as the 'bitless bridle'. From the limited evidence currently available it is not possible to establish the efficacy of different conservative measures and further studies are therefore warranted.

5.6.3 Effect of study quality on results

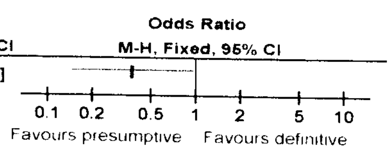
It is probable that several factors relating to study quality may influence the reported results. This systematic review permitted preliminary conclusions to be made for diagnosis, outcome measure and previous surgery. It was not possible to determine how the proportion of horses which underwent the procedure and were not included in the final analysis affected the results.

Effect of inclusion criteria: presumptive or definitive diagnosis

There was variation between studies as to whether only DDSP was assessed or whether palatal dysfunction (PI or DDSP) was assessed and how the diagnosis was made. Many studies relied on a presumptive diagnosis of DDSP based on clinical history and/ or resting endoscopic findings. Definitive diagnosis was possible only through the use of exercising endoscopy. However, there was variation between studies as to whether PI was ever diagnosed, whether PI was considered presumptive of DDSP or whether PI and DDSP were grouped together and considered to be definitive of palatal dysfunction.

Franklin *et al.* (2009a) found no significant difference in the success rates between horses diagnosed with DDSP and those diagnosed with PI during treadmill endoscopy. Similarly, in the study by Woodie *et al.* (2005a) there was no significant difference in results between horses with a definitive diagnosis of DDSP and those with a presumptive diagnosis based on history and resting endoscopy or history alone. However, in a subsequent study by the same group (Cheetham *et al.* 2008) horses with a definitive diagnosis of DDSP were less likely to race post-operatively compared with horses that had a presumptive diagnosis. Only 66% of definitively diagnosed cases raced post operatively where as 84% of presumptively diagnosed cases raced post operatively, and the analysis performed for this review showed that having only a presumptive diagnosis significantly favoured post operative racing (figure 5.1). The presumptive diagnosis category comprised horses in which treadmill endoscopy was not performed (81%) and horses in which PI, but not DDSP, was observed during treadmill endoscopy (19%). Although firm conclusions cannot be made it is possible that success rates may be lower when only definitively diagnosed cases are reported.

	Definitive		Presumptive		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	M-H, Fixed, 95% CI
Cheetham et al 2008	24	36	59	70	0.37 [0.14, 0.96]



5.1 Forest plot showing success rate for the definitively diagnosed group compared with a presumptively diagnosed group. The results suggest that having a presumptive diagnosis significantly favours having a post-operative start

Effect of outcome measure

There were wide variations in the outcome measure used and some studies used many outcomes. There is some evidence that the outcome measure may have a substantial effect on the reported results.

Return to racing (i.e. a postoperative start) may not be the most appropriate indicator of a successful surgical outcome. Several authors reported the proportion of horses that return to racing and then provided a more stringent definition of success (i.e. increased earnings) (Barakzai *et al.* 2004, Barakzai and Dixon 2005, Barakzai *et al.* 2009a, Duncan 1997, Dykgraaf *et al.* 2005, Franklin *et al.* 2009a) (table 5.2). In all cases the proportion of horses considered to be successfully treated was substantially lower (up to 48% lower) than the proportion that returned to racing, showing that a post operative start may be an optimistic measure of success.

Table 5.2 Differences in results where post operative start is the measure of success compared with those using a different race performance outcome as a measure of success

	Percentage of horses that raced post operatively	The trial authors determination of success using a different race performance outcome (%)	Percentage difference
Barakzai *et al.* 2004	92.5	60	32.5
Barakzai and Dixon 2005	94	61	33
Barakzai *et al.* 2009a	83 93	35 53	48 40
Duncan 1997	94	70	24
Dykgraaf *et al.* 2005*	88	62	26
Franklin *et al.* 2009a*	96	48	48

*results from combined interventions

The way race performance is assessed may also substantially affect the apparent success rates (Reardon *et al.* 2008a &b; Barakzai *et al.* 2009a; Franklin *et al.* 2009a). Success rates may be affected by race parameter used as well as the number of races. Reardon *et al.* (2008a) showed a significant, but very weak correlation between ratings and earnings, and found significant differences between ratings and performance index and earnings and performance index. This resulted in variation in success rates (28-51% and 42-67%) when different parameters were examined over the same time period (Reardon *et al.* 2008a &b). The number of races assessed before and after an intervention also had an effect on the reported success rates (Barakzai *et al.* 2009a; Franklin *et al.* 2009a). Franklin *et al.* (2009a) showed that the effect of multiple variations is racing parameters was considerable. When using the same horse data, but varying between ratings and earnings, together with varying the number of races used, the apparent 'success rate' varied widely from 32-59%, 26-62% and 38-73% for three different interventions.

For subjective outcome measures (by trainer questionnaire) results may vary depending on the question asked and individual opinion in what constitutes success. In one study 72% of horses were considered by the trainer to be successfully treated (Ordidge 2001). However, if success was more strictly defined to be 'cessation of gurgling noise' only 48% of the horses that were reported to make 'gurgling' noise pre surgery would be considered to be successfully treated.

Only one study included both subjective assessment and objective assessment using race performance in a similar population of horses (Woodie *et al.* 2005a). The reported success rates were very similar (86% for subjective methods and 82% for objective methods). In contrast subjective trainer assessment had no correlation with improvement in upper airway function assessed by repeat treadmill endoscopic examination (McCluskie *et al.* 2009). However when repeat endoscopy is used as an outcome measure this may also lead to variation in apparent success rate because it is uncertain what level of palatal stability should constitute a successful outcome (McCluskie *et al.* 2009).

Confounding variables (previous surgery)

Woodie *et al.* (2005a) found no effect of prior surgery on the trainers' assessment of performance. However a significant improvement in performance index was found in horses which had not undergone previous surgery compared with those in which there had been previous surgical interventions (Woodie *et al.* 2005a). In contrast, Parente *et al.* (2002) suggested there was a significant association between previous surgery and a positive performance outcome.

5.7 Discussion

This is the first systematic review in the area of equine dynamic URT disorders. Numerous difficulties were encountered and undertaking evidence-based veterinary medicine is challenging due to a "serious lack of high-quality patient centred veterinary research" (Murphy 2002).

Systematic reviews should contain studies of the highest available level of evidence. Well-conducted randomised controlled trials are the preferred study design because they are least likely to be biased (Reeves *et al.* 2008) but have been avoided in equine veterinary practice because of methodological, financial and ethical constraints (Murphy 2002). Therefore the inclusion criteria were widened to level ≥ 4 evidence to more fully consider the current evidence base. Broad inclusion criteria were used (Stroup *et al.* 2000), with the aim of analysing differences in the study designs and their relationship to the reported outcomes.

This systematic review included all relevant studies regardless of publication status, with independent assessment of study quality. All the included studies had been peer reviewed, however the stringency of this process is likely to vary between (and within) journals and conferences. Other veterinary systematic reviews have restricted inclusion criteria to peer reviewed journals (Olivry and Mueller 2003; Nuttal and Cole 2007). It has been suggested that studies that have not been peer reviewed may have unreliable results (Chalmers *et al.* 1987). However, publication bias (Meakins 2002) is thought to be greatest for small non-randomised studies (Newcombe 1987; Easterbrook *et al.* 1991; Dickersin and Min 1993). Therefore guidelines from the Cochrane collaboration (www.cochrane.org) and Centre for reviews and dissemination (www.york.ac/inst/crd/) suggest that reviews should aim to include all relevant studies, regardless of publication status. In human systematic reviews it is also important to identify duplicate publications. Pharmaceutical companies may publish the results of one clinical trial several different times. This is likely to be less prevalent in equine medicine and surgery. However, several studies in this systematic review did contain an overlap of a small number of cases (Woodie *et al.* 2005a and Cheetham *et al.* 2008; Barakzai and Dixon 2005 and Barakzai *et al.* 2009a; Franklin *et al.* 2009a and McCluskie *et al.* 2009).

Search strategies used widely in the medical field (Haynes *et al.* 1994) may not be effective for locating veterinary literature (Murphy 2002; 2003). Therefore a broad search query was used (Olivry and Mueller 2003; Aragon *et al.* 2007; Nuttal and Cole 2007). PubMed yielded relatively few results, whereas the other electronic databases yielded large numbers of irrelevant studies, confirming that no one database provides comprehensive indexing to all relevant veterinary literature (Murphy 2002).

Development of the inclusion criteria proved problematic. The initial aim was to assess mutually exclusive interventions only. However after initial review of the database it became clear that for many studies variation in the interventions undertaken was present. Formulating a question that strikes a justifiable balance between the ideal and the feasibility of answering the question is important (Haynes 2006a). Hence the inclusion criteria were redefined, with the aim of more fully understanding the evidence base, particularly for interventions currently being performed. Due to the limited studies assessing conservative techniques, studies were permitted when the results of different conservative procedures were presented as one result. For surgical interventions involving myectomy / tenectomy, tension palatoplasty or laryngeal tie-forward, variation in the surgical technique was allowed. Sub-epiglottic resection performed in conjunction with any tension palatoplasty procedure was classified as variation in technique. This was described as part of the original technique (Ahern 1993a) but has subsequently been omitted by some surgeons. Furthermore, where studies combined the results from horses undergoing tension palatoplasty with and without sub-epiglottic resection, statistical analysis was performed prior to grouping and showed no significant difference in success rates (Franklin *et al.* 2009a). It was also decided to permit laryngeal tie-forward with and without sternothyroid tenectomy as variation in technique, because both of these procedures affect rostral positioning of the larynx. Sternothyroid tenectomy was not described in the original study (Woodie *et al.* 2005a) but was described as a modification of the technique later (Ducharme 2005). Again, a statistical analysis showed no significant difference in success rates between groups (Franklin *et al.* 2009a). However sternothyroid tenectomy performed in conjunction with another form of surgery (e.g. tension palatoplasty) was classified as a separate technique because it would not be possible to determine whether the results might arise due to alterations in laryngo-hyoid positioning or changes in the tension of the palatal tissues themselves. The original more stringent inclusion criteria would have resulted in exclusion of the majority of studies in which a definitive diagnosis was achieved (Barakzai and Dixon 2005, Cheetham *et al.* 2008, Barakzai *et al.* 2009a, Franklin *et al.* 2009a and McCluskie *et al.* 2009). As better studies become available for all interventions, the inclusion criteria should be more strictly defined in future reviews.

For this review the inclusion criteria were also restricted to naturally occurring cases of DDSP. The authors believed that it was not appropriate to include studies of experimentally induced DDSP, because the underlying cause of this condition remains unclear. There were also many, often well-conducted, experimental studies on normal horses that were excluded from this review.

In this systematic review, an English language text had to be available for inclusion. Four of the 76 exclusions were because an English language text was not obtained therefore the suitability of the article for inclusion could not be assessed. It should be noted that ideally all languages should be included.

Quality assessment indicates the likelihood that the results are a valid estimate of the truth (Moher *et al.* 1995). Differences in study quality may explain the heterogeneity in the results. Study quality assessment checklists developed for human studies were not suitable for this review, therefore a quality assessment checklist was developed to identify the main potential limitations for each study. However, it is still unknown which of these criteria are the most important in establishing study quality. Hence for studies which fulfil different criteria it remains unclear which represents the better quality study.

Most studies in this field are before-and-after studies reporting pre-and-post intervention data. Other studies used the same approach of describing pre-and-post intervention data but have also used a comparison group, such as a different intervention (parallel group study). Several authors described studies as case-control studies whereby pre and post intervention data for 'cases' (diagnosed with DDSP) was compared to the same data for 'control' horses (not diagnosed with DDSP). The ideal 'control' group for intervention studies is cases with DDSP which undergo no treatment (Cheetham *et al.* 2008; Barakzai *et al.* 2009a). As this is difficult to achieve, it was suggested that the 'control' group could be unaffected horses. However in no study was any attempt made to confirm the 'controls' were DDSP negative and therefore were a valid comparison. Furthermore, knowledge of the outcome status before collection of exposure information is the defining feature of a case-control study (Fosgate and Cohen 2008). It has previously been suggested that these studies should not be classified as case-control studies (Fosgate and Cohen 2008); therefore for the purposes of this review were reclassified cohort studies.

There are difficulties in grading the level of evidence of veterinary studies as several different systems have been published and as yet there is no clear consensus (Innes 2007). Furthermore, many of the levels of evidence guidelines developed for human evidence based medicine do not fully include or differentiate the types of study included in this review. It has been argued that both hierarchies of study design and common sense judgment be used when assessing quality of research studies (Greenhalgh 2010). Hence, although it was difficult to rank individual studies, we generally considered studies in which a comparator group was used to be a better study design than a case series.

A problem with many studies is the lack of a definitive diagnosis prior to treatment. Results of studies conducted in which horses were not confirmed to have the disorder being investigated are potentially misleading. It was not possible to fully confirm to what degree this affected the results. However the results of one study suggested that success rates may be lower in horses with a definitive diagnosis than those with a presumptive diagnosis. Several studies have documented that respiratory noise, resting endoscopy findings or both in conjunction may be unreliable in predicting dynamic events that occur during exercise (Morris and Seeherman 1991; Kannegieter and Dore 1995; Martin *et al.* 2000; Tan *et al.* 2005; Lane *et al.* 2006b; Witte *et al.* 2010; Barakzai and Dixon 2011). However, two studies did demonstrate that the specificity of DDSP during resting endoscopy was high (Lane *et al.* 2006b, Barakzai and Dixon 2011); therefore intervention studies based on this criterion would have a low proportion of false positive diagnoses (Barakzai and Dixon 2011). It should be noted that most of the included studies used broader inclusion criteria based on resting endoscopy and history findings, and only two studies required all horses to demonstrate DDSP during resting endoscopy for inclusion (Duncan 1997, Reardon *et al.* 2008a). The low sensitivity of DDSP at rest (Lane *et al.* 2006b, Barakzai and Dixon 2011) should also be considered. Studies based on this criterion would include only a small subset of cases, and it is unclear whether these are representative of the wider population of horses experiencing DDSP during exercise, or whether these cases might be more severely affected. Further clarification as to whether PI and DDSP are manifestations of the same condition is also important. Ideally intervention studies should be based on horses confirmed to have the disorder being investigated.

It is also important to confirm absence of other forms of dynamic URT collapse, because this may have an impact on subsequent success rate. The prevalence of complex URT collapse is high (Tan *et al.* 2005; Lane *et al.* 2006a; Barakzai and Dixon 2011) and any additional forms of URT collapse tend not to be addressed in horses which do not undergo exercising endoscopy. With palatal dysfunction this may be complicated by the potential link between palatal dysfunction and axial deviation of the aryepiglottic folds (Parente *et al.* 1994; Tan *et al.* 2005; Ahern 2005a; Lane *et al.* 2006a).

No study assessed co-interventions. The concurrent use of conservative measures such as a tongue tie following surgical treatments for DDSP (Barakzai *et al.* 2009b) may influence results. Other management changes are also likely to be important when race performance is used as the outcome measure. Confirmation of a diagnosis of DDSP and associated veterinary advice may influence trainers' management of cases. Previously performed URT surgeries may also be a confounding variable and were encountered in several studies (Ordidge 2001, Parente *et al.* 2002; Barakzai and Dixon 2005; Smith and Embertson 2005; Woodie *et al.* 2005a), although the results were contradictory as to whether previous surgery had a positive or negative effect.

The way in which success is measured appears to have the greatest effect on the reported results. Outcome measures should be valid, consistent and accurate for the condition being investigated. At present there is a degree of uncertainty of the accuracy of the outcome measures used. Outcome measures used in veterinary surgery are starting to receive more attention (Brown 2008) and it has been suggested that whether the outcome measure is subjective or objective is not as critical as whether it is valid and reliable (Brown 2008). Furthermore, it is important that investigators define what constitutes treatment success or failure a priori, and that a limited number of such measures should be used, or steps be taken to reduce the risk of Type I error where multiple outcomes are considered.

Subjective measures of success by the trainer may provide useful information. However, it is unclear whether improvements in upper airway function can be accurately detected by a trainer's assessment of changes in respiratory noise and/or performance. In contrast to more objective measures, subjective assessment usually involves a retrospective pre post intervention assessment and memory decay and even a placebo effect may affect results. It is also likely that trainers' perceptions of success may vary between horses. This review shows that it is important that questions are well formulated and specific.

Although the value of using race performance data may be justified as owners aim for improved racing performance, there are several elements that may make these results unreliable. The inference is that improved racing performance occurs because of improvements in URT function. However, racing performance is multifactorial and the multifactorial nature of poor performance and the high prevalence of complex forms of URT collapse will also influence subsequent racing performance. Also, differences in results between studies may be largely introduced by the different population of racehorses referred to each centre (Beard and Waxman 2007).

This review showed that the use of post operative start as an outcome measure results in high 'success rates'. However it is likely that this is a weak indicator of success, simply because in many cases abnormal respiratory noise or poor performance only occurs during racing, therefore trainers have to enter the horse in a race to determine whether the intervention was successful. Cheetham *et al.* (2010) also suggested that the decision to use 'starts' compared with earnings as an outcome measure could have a marked effect on reported success rates. This systematic review also showed that large variations in success rates were observed when the race performance measure and number of races assessed is altered, and this casts serious doubt on the validity of this outcome measure. Furthermore as race performance is often converted to a binomial outcome, it is unclear to what degree the results remain clinically relevant. For example, a horse only needs to earn £1 more after the intervention than before to be grouped in the success category. In a recent study from North America it was suggested that age, breed, sex, track surface and gait should be controlled for in the study design and analysis of race performance following an intervention (Cheetham *et al.* 2010). It is unclear whether there are other factors such as handicapping that should also be accounted for.

From a veterinary perspective, the use of repeat exercising endoscopy is probably the most sensible method to determine the efficacy of an intervention. Understanding how an intervention alters the structure and function of the pharynx in naturally occurring disease is of great importance, and further studies undertaking this approach should be encouraged. Even so it remains unclear to what extent palatal function should be restored to constitute success. DDSP is an intermittent event, hence where PI occurs post-intervention it remains unclear as to whether this truly reflects resolution of DDSP or whether DDSP might occur during subsequent runs or under different exercise conditions. It is important that the same exercise test is undertaken pre and post intervention and for results to be clinically relevant the exercise test should be representative of racing. Studies which evaluate the repeatability of DDSP under the same exercise test conditions are required before this method is truly valid. Unfortunately, smaller numbers of horses are likely to be included than for subjective or race performance studies. The development of overground endoscopy may better enable these studies, however it is critical that exercise test design is appropriate.

In some studies, there were large differences in the number of horses that underwent the procedure and the number that were subsequently analysed. The greater this difference, the greater the potential for inaccurate results due to introduction of bias. The use of racing performance results in many cases, which have undergone the intervention, being excluded from the analysis as many horses will not have completed the requisite number of starts pre and post intervention. This method likely creates a bias towards cases in which the intervention was successful, as cases in which the treatment was unsuccessful are less likely to continue racing. Recruiting cases for endoscopic studies is also difficult and inappropriate recruitment may introduce the opposite bias into the results, due to the possibility of poorly performing horses being more likely to be presented for reassessment. It is important that in the study design methods to reduce inclusion bias are taken. Furthermore reasons for all exclusions should be specifically described. Substantial research needs to be undertaken on which outcome measures provide the most clinically relevant information and these should then be standardised between studies.

Systematic reviews only include efficacy studies in clinical cases, therefore several research studies which provide evidence to support or refute an intervention are not discussed in this review. However, in the author's opinion the disparity of the conclusions between experimental studies on normal horses and efficacy studies in clinical cases needs addressing.

The ability to draw conclusions regarding the potential treatment harms was also severely restricted due to under-reporting. As well as assessing short term complications associated with surgery, it is necessary to investigate whether procedures fail to resolve palatal dysfunction and whether procedures result in worsening of this condition or induce any additional forms of upper airway collapse.

Several systematic reviews have been undertaken in the human field for snoring and obstructive sleep apnoea, and the results are not dissimilar to those identified here. A search of the Cochrane database revealed at present there is insufficient evidence to support the use of surgery in OSA (Sundaram *et al.* 2005) or drug therapy in the treatment of OSA (Smith *et al.* 2006). There is limited evidence to support the use of corticosteroids in children with OSA (Kuhle and Urshitz 2011). In a Cochrane review of the effects of lifestyle changes (i.e. exercise) on OSA, no trials were even identified (Shneerson and Wright 2001). Other systematic reviews for snoring and

OSA also suggest that there is no evidence of effect for some surgical interventions and furthermore that half of the patients undergoing uvulopalatoplasty or uvulopharyngoplasty experienced persistent side effects (Franklin *et al.* 2009b). Most reviews are limited by the paucity and poor quality evidence available and suggest the need for randomized controlled trials and of standardising of outcome measures (Main *et al.* 2009).

Research synthesis in this review has been severely limited because of the heterogeneity in the included studies. The systematic review suggests that factors relating to study methodology may have an important impact on the reported efficacy of procedures and therefore the accuracy of the results. Whilst more recent studies have attempted to overcome weaknesses of earlier studies, substantial limitations still often exist. Overall, the low level of evidence makes it difficult to draw firm conclusions as to the efficacy of procedures for DDSP. Hence it is currently not possible to determine which procedure is the most appropriate. The intent of a systematic review is not to belittle individual studies. Rather, the purpose is to establish the limits of the current evidence base which will allow future studies to target these areas. This systematic review has highlighted the difficulties of studying palatal dysfunction. Whilst many of these may not be readily overcome, the review highlights areas where improvement can be made and underlines the need for high quality studies, rather than just more studies.

Chapter 6 Conclusions of the current evidence base.

Previous chapters have shown that there is only a limited evidence base for equine dynamic palatal dysfunction. There have been several studies assessing diagnostic techniques and generally the results suggest that in order to obtain an accurate diagnosis of this condition and to exclude other similar conditions endoscopy during exercise should be performed. There is currently poor experimental evidence to fully explain the aetiopathogenesis of this condition, which has clearly impacted on the efficacy of treatments available. Therefore there are huge limitations to veterinarians practicing evidence based medicine in this field.

By examining the evidence for the diagnosis, aetiopathogenesis and treatment a comprehensive understanding of the current evidence base for this condition has been developed. Therefore where good evidence has been identified this can be fed back to improve clinical practice. For areas where insufficient evidence has been identified, the previous chapters have highlighted the gaps in our knowledge base which are then fed back into the research agenda.

Although the value of high speed treadmill endoscopy has been shown, there remain concerns as to whether this technique truly replicates racing. Questions persist particularly for horses in which 'gurgling' is reported but DDSP does not occur, and whether the inaccuracy lies with the trainer or with this technique. As a result development of a field based diagnostic technique would be of value. Furthermore a better understanding of exercise testing is required. The effect of incline, speed and exercise duration on airflows and upper airway pressures needs further study, so that appropriate protocols can be developed for both flat and NH horses. It is also critical to understand the repeatability of DDSP under the same exercise test conditions and also under different exercise test conditions. The effect of DDSP on ventilation has been studied in a small number of cases, but the effect of PI needs more understanding. It is also necessary to establish whether PI is part of the same syndrome as DDSP and what degree of palate stability is normal or optimal. It is also important to be aware of the benefits versus the risks of diagnostic techniques. The risk of injury during exercise should be understood. Clearly the benefit of a diagnostic technique should be to improve horse welfare by providing targeted treatment. Certainly no diagnosis by itself ever made a patient better and the ultimate proof of a diagnostic tests value lies in the outcomes of the patients who submit to it. Unfortunately current evidence from the systematic review suggests that the prognosis for horses with a definitive diagnosis is in fact worse! At present it is unclear whether horses with a definitive diagnosis are managed differently or whether this finding just confirms that a substantial proportion of the presumptive category did not have the condition being treated. The value of obtaining a definitive diagnosis is reduced because of the poor efficacy of treatments. If we wish to improve the health and welfare of horses a better understanding of the aetiopathogenesis and improved treatments are imperative.

The diagnostic assessment should also establish severity, identify optimal treatments and likely responsiveness to therapy. However, there is a complete lack of evidence in these areas. Selection of surgical procedures is intuitively a critical step in the process, yet little data exist on how this process occurs. Selecting an intervention appears to be the surgeon's preference based on empiric experience, training and ability and is not based upon evidence based data.

It is clearly imperative to have a substantially improved understanding of the aetiopathogenesis of this condition. It is important to establish whether this is the same for all horses or whether there are numerous predisposing factors for which DDSP is an end point. Research is needed to clarify whether this is a pathological condition or whether it is a physiological phenomenon in athletic horses i.e. a consequence of reaching their performance limit. Only when the aetiopathogenesis is better understood is it likely that effective treatment and prevention strategies will be developed.

It is important to fully understand how interventions address the aetiopathogenesis, and how they affect the structure and function of the URT. Certainly more effective treatments appear to be required and adverse effects need to be better understood. Treatment selection has been largely ignored and it is important to understand whether all horses should be advised the same treatment or whether there are targeted treatments for certain individuals. Furthermore better quality intervention studies need to be performed. Prior to undertaking any more intervention studies, considerable research on study design and outcome metrics is required. There also appears to be poor correlation between the different metrics. Knowledge is limited as to what outcome measure should be used to describe the physiology of the disease process and predict the outcome of therapy.

Finally the barriers to translating evidence based information into clinical practice have received no attention.

The ultimate goal is to improve the health and welfare of racehorses by being able to accurately diagnose and successfully treat and prevent this condition. The condition is a source of frustration amongst veterinary surgeons and trainers. Now that the evidence has been comprehensively reviewed key areas, such as diagnosis and outcome, have been identified to which further studies can be targeted. In section 2 of this thesis, six primary research studies were undertaken with the aim of improving our understanding of this condition by commencing research to target gaps in the evidence base.

Part 2

Publications:

Clinical trials using a telemetric endoscope for use during over-ground exercise: A preliminary study. *Equine vet. J.* 40, 712-715.

Comparisons of overground endoscopy and treadmill endoscopy in U.K. Thoroughbred racehorses. *Equine vet. J.* 42, 186-191.

Assessment of the exercise tests used during overground endoscopy in UK thoroughbred racehorses and how these may affect the diagnosis of dynamic upper respiratory tract obstructions. *Equine vet. J. suppl.*, 38, 587-591.

Chapter 7 Development and preliminary clinical trials of an overground endoscope

7.1 Introduction

Dynamic collapse of the upper respiratory tract occurs when the soft tissue structure(s) are unable to withstand the high inspiratory pressures that occur during exercise and therefore collapse into the airway creating an obstruction to airflow. Structures of the nasopharynx and larynx are most commonly affected and numerous disorders have now been described in the literature (Kannegieter and Dore 1995; Martin *et al.* 2000; Morris and Seeherman 1991; Tan *et al.* 2005; Lane *et al.* 2006a; Franklin 2008). Several studies have documented that these disorders cannot be accurately diagnosed during a resting endoscopic examination (Kannegeiter and Dore 1995; Parente and Martin 1995; Tan *et al.* 2005; Lane *et al.* 2006b, Barakzai and Dixon 2011). Therefore endoscopy during exercise is typically required to establish a definitive diagnosis. To date, the only method available has been to perform an endoscopic examination during high-speed treadmill exercise (TM). Unfortunately the cost, time implications and misconceptions regarding the safety of the technique mean that this is not always performed and many horses receive a diagnosis on the basis of history of abnormal noise and resting endoscopic findings. Although currently an endoscopic examination during TM exercise is considered to be the gold standard technique for assessment of dynamic URT collapse, it is well known that treadmill exercise does not replicate exercise in the field, and therefore there is the potential for misdiagnosis with this technique also. There are significant differences in heart rate, blood lactate, stride frequency and stride length between field exercise and treadmill exercise (Barrey *et al.* 1993a and b; Sloet van Oldruitenborgh-Oosterbaan and Barneveld 1995; Courouce *et al.* 1999; Sloet van Oldruitenborgh-Oosterbaan and Clayton 1999; Courouce *et al.* 2000; Evans 2004). So much so that Evans (2004) concluded that design of a treadmill exercise test to replicate field exercise was a fruitless endeavour. Therefore it would be advantageous to perform endoscopy of the URT whilst the horse is exercising in its normal environment.

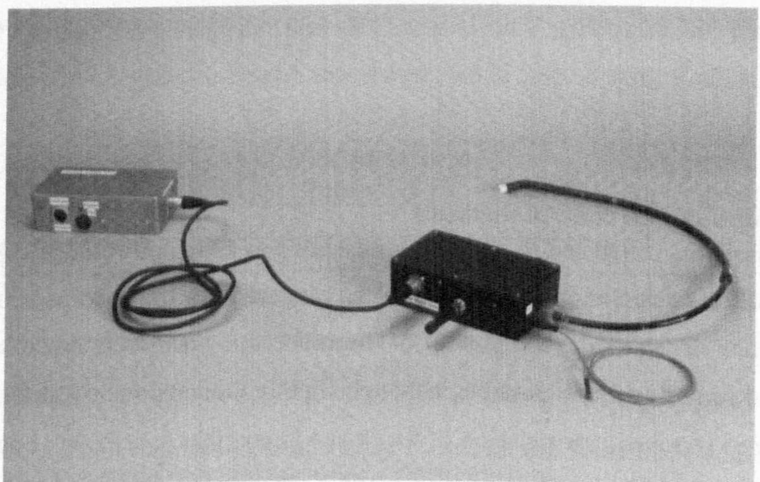
This chapter describes the development and preliminary clinical trials of a telemetric endoscopy system which can be used to image the URT during lunged or ridden exercise in the field.

7.2 *Development of the endoscopy system*

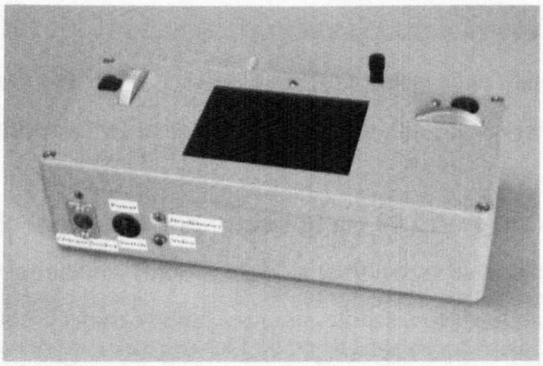
The telemetric (overground) endoscope used was developed by the Department of Electrical Engineering at the University of Bristol, under the guidance of Dr Samantha Franklin MRCVS.

The insertion tube[3], which measured 90 cm in length with an external diameter of 1.2 cm, was incorporated into a head mounted box (19cm x 11cm x 6cm) containing the image transmission and control equipment, with leads to a saddle-mounted battery pack (19cm x 11cm x 6cm) (figure 7.1). The total weight of the system was 2.25kg. The head-mounted box weighs 1.05kg and the battery box a further 1.2kg.

Positioning of the endoscope tip was achieved by wireless control. The endoscopy image was transmitted to a hand-held control box (figure 7.2) by radio-telemetry for viewing in real-time.



7.1 Photograph showing the endoscope and microphone attached to the head-mounted endoscope box with the lead supplying power from the battery box



7.2 The control box which incorporates a screen for image viewing and the endoscope controls

7.3 Preliminary equipment testing

7.3.1 Battery duration

Three tests of battery duration were performed. Following an 8-hour recharge excellent quality transmission lasted for on average 1 hr 45 min. This was considered satisfactory to perform a clinical assessment in 3 or 4 horses, if the device was turned on only for the duration of the exercise test.

7.3.2 Transmission and control distance

A simple field trial was conducted to assess the transmission and control ranges. An attenuator can be placed on the transmission aerial to unify the ranges. With the attenuator in place good quality transmission of the image and control of the endoscope position is possible over 130m. Transmission and control was still possible, although slightly impaired up to a distance of 170m. With the attenuator removed, transmission of the image is possible over 220m, however control of the endoscope position is possible only over 100m. This information should be considered when deciding upon the location for performing overground endoscopy. For the clinical trials, the attenuator was removed to achieve the greatest distance of image transmission.

7.3.3 Light output tests

The light transmission of the telemetric endoscope was compared to a traditional endoscope used for high-speed treadmill video endoscopy[4]. The endoscopes were inserted into a light proof tubing and the light output measured at a distance of 8cm from the tip of the endoscope. The measurement was repeated on three separate occasions. The traditional videoendoscope (with a

100W xenon light source[5]) had a mean transmission of 680 lux. However, the telemetric endoscope had a mean transmission of only 270 lux. Therefore the light output of the telemetric endoscope is considerably lower than from a traditional videoendoscope which may compromise the diagnostic quality of the images.

7.3.4 Heat production at endoscope tip

A significant amount of light energy is converted to heat. With traditional videoendoscopes, the xenon light source is located within the video processor and the light is transmitted to the endoscope tip by fibres, therefore the light source does not come in contact with the horse. However with the overground endoscope the light source is from LEDs placed at the endoscope tip. Patient safety is crucial for all procedures, and it is important to ensure that the temperature of the endoscope tip is not high enough to cause thermal injury of the URT mucosa. The temperature at the endoscope tip was measured with a laser thermometer gun. The tip of the traditional videoendoscope was used as a control. Both endoscopes had been switched off >12 hours prior to starting. Three temperature measurements were obtained at each time point and the mean temperature calculated.

Time (mins) constant use	Videoendoscope Mean temperature (°C) at tip	Overground endoscope Mean temperature (°C) at tip
0	19.1	18.1
10	19.8	19.7
20	20.4	20.1
30	22.3	22.1

The results show a small increase in temperature over both endoscope tips with continued use. However even after 30 minutes of constant use the temperature rise was minimal and was not considered high enough to cause any thermal injury. The results also show that placing the light source (LED's) at the endoscope tip did not result in substantially greater temperatures than with a traditional videoendoscope.

7.3.5 Imaging the upper respiratory tract

The initial assessment of this system revealed insufficient downward steering of the endoscope. At this stage the downward flexion was only 30 degrees, and it was not possible to view the ventral larynx or nasopharynx. However, the upward and left /right steering were considered sufficient. The equipment was subsequently adjusted to its maximum capability, increasing the amount of downward flexion at the endoscope tip to 40 degrees. Further assessment revealed that this degree of downward flexion appeared sufficient (figure 7.3).

7.3 Endoscopy image showing the maximum downward rotation of the endoscope tip. The epiglottis and soft palate can be clearly seen.

7.3.6 Mounting the system onto the horse

The practicalities of mounting the system onto the horse were assessed. The overground endoscope was developed with the idea of attaching the box to a mask similar to that used for treadmill endoscopy at the University of Bristol (figure 7.4). Therefore the endoscope box was mounted onto the front of the horse's head.

7.4 Image of mask used during high speed treadmill endoscopy. The mask secures the endoscope and also permits recording of respiratory noise and the placement of flow tubes for measurement of respiratory parameters

Although diagnostic images of the upper respiratory tract were achieved, the system proved difficult to secure and frequently slipped downward. In addition, subjectively the horse appeared to resent this, and frequent head-shaking was observed. The position of the box and the degree of head-shaking were thought to pose a risk to handlers. The resentment by the horse and the concerns of even handling the horse on the ground, led to the conclusion that it was unlikely to be safe to exercise under saddle with this system.

Alternative methods of mounting the system were discussed. Mounting the endoscope box between the eyes, at the poll, on the side of the face, and on the neck were all trialled and rejected. The most appropriate method involved mounting the system underneath the mandibles. This resulted in the least amount of head-shaking by the horse, and was deemed safest for the handlers/jockey.

A custom built headpiece was developed. This involved an adjustable hood worn by the horse in which the endoscope box secured in a pouch can be attached underneath (figure 7.5). In addition, a custom-made saddle cloth was made to hold the battery box, recording device and leads safely.

7.5 Photograph showing the custom-made headpiece securing the endoscopy system

7.3.7 Microphone

The microphone was trialled attached to the face mask, just above the nostrils. However the sound recording was unsatisfactory and generated an artificial mechanical noise, which was considered unrepresentative of URT sounds and was therefore non-diagnostic. The microphone was not used on any further trials.

7.3.8 Recording of the image

Recording of the image was possible both on the horse and remotely. The endoscopy image was recorded directly on the horse, onto a miniature digital video recorder. Recording of the image was also possible remotely, from the control box. However, it was considered appropriate to record directly from the horse for two reasons. Firstly the recorded image will not be affected by transmission interference. Secondly, if the horse exercised beyond the transmission capabilities of the system, diagnostic images would still be achieved, albeit reviewed at a later time. Two types of miniature digital video recorders were tested[67] and good quality recordings were made from both types on lunged horses, however, only the solid-state recorder[7] could record good quality images at gallop. For the further clinical trials it was decided to use two recorders to ensure a back-up recording was always available.

7.4 Preliminary clinical trials

7.4.1 Materials and Methods

Overground telemetric endoscopy was performed on 15 horses, presented for abnormal respiratory noise or poor performance. Eleven horses were Thoroughbred racehorses, two were used for eventing and the remaining two for general riding purposes. In all horses the equipment was mounted in the stable, and the horse was warmed-up with the equipment in place. Nine horses were exercised at trot and canter on the lunge in an indoor school (20m x 60m) (figure 7.6). Subsequently, six of these horses underwent video-endoscopy during an incremental standardised exercise test to fatigue on a high-speed treadmill and the results of both procedures were compared. A further six horses were exercised by their normal jockeys at canter and gallop speeds (up to 38mph) at two training premises (figure 7.7). The exercise was performed on a straight, inclined, all-weather gallop (either 5 or 6 furlongs) and the veterinary surgeon with the handheld control box travelled in a car alongside the gallops. In one horse, a five furlong circular gallop was also performed, and in this case the veterinary surgeon remained in the centre of the circle.

7.6 Telemetric endoscopy performed during lunged exercise in an indoor school

7.7 Photograph taken from within a car showing a horse exercising at gallop with the endoscopy system in place. The image is transmitted to the hand-held control box, for viewing in real time by the veterinary surgeon

All horses were assessed subjectively to identify any alteration in behaviour, position of head and neck during exercise, gait or willingness to exercise that occurred as a result of the equipment. The horses that undertook lunged exercise were assessed with and without the endoscope in place. For the six horses ridden on the gallops, the jockey was questioned following the procedure. The video recordings from the on-horse recorder were downloaded onto a PC following exercise and the diagnostic quality of the image was assessed subjectively.

7.4.2 Results

No alteration in gait or willingness to exercise was observed in any horse. However some horses were observed to 'snort' more than usual due to the presence of the endoscope. Two horses were observed to shake their head at the start of exercise. However, once exercise was established, no alteration in head carriage was observed in any horse (table 7.1).

Diagnostic quality images of the larynx and nasopharynx were obtained in all horses.

For the horses exercising in the indoor school, images were obtained regardless of the position of the horse or veterinary surgeon. On occasion the image quality on the hand-held control box was slightly impaired due to intermittent loss of signal. This was likely due to interference from signal reflection off the metal roof. The image quality was unaffected when the recording was obtained directly on the horse.

For horses exercising up a straight gallop, excellent images were obtained for the entirety of the gallop whilst the veterinary surgeon was travelling alongside. Similarly diagnostic images were achieved when the veterinary surgeon was positioned in the centre of a five furlong circular gallop.

In almost all cases, the presence of mucus on the camera at the endoscope tip impaired image quality on occasion. In some cases the mucus was removed if the horse swallowed, however in other cases the endoscope required removing, cleaning and replacing.

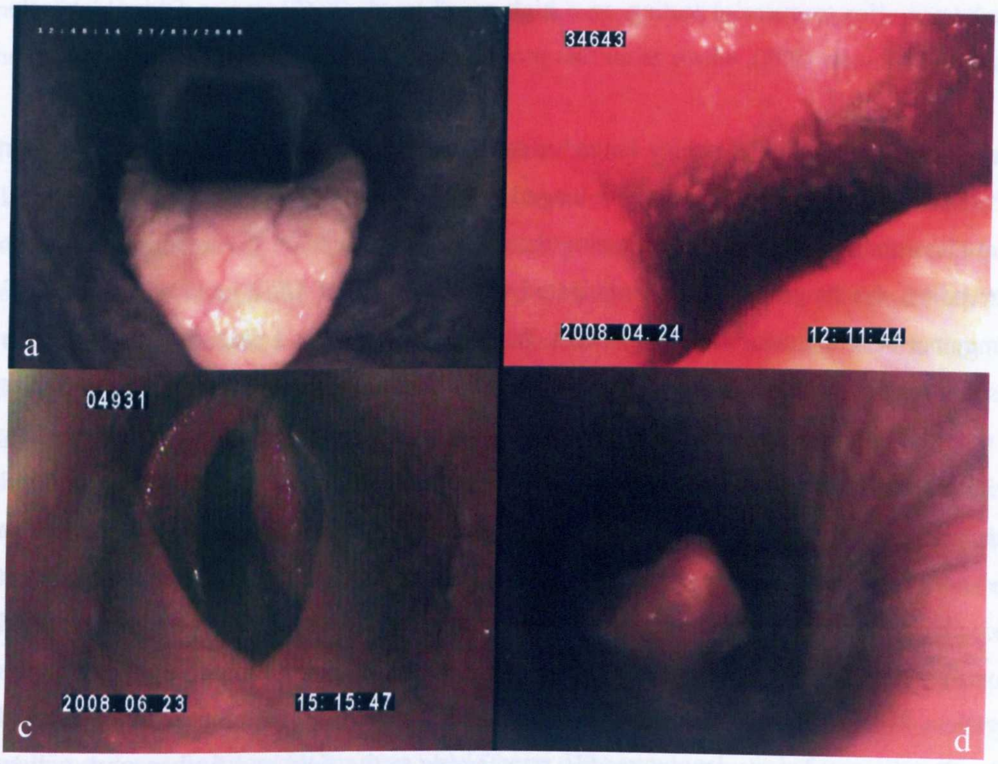
In 12 horses some form of abnormality of the URT was observed. Six horses had telemetric endoscopy performed during lunged exercise and routine video-endoscopy performed during TM exercise the following day. In four of these six horses abnormalities of the URT were observed during lunged exercise (table 7.1, figure 7.8). However in all six cases additional abnormalities were observed during more strenuous exercise on the treadmill (table 7.1). Dynamic airway collapse was also observed in five out of six horses examined on the gallops (table 7.1, figure 7.8).

Table 7.1 Results from 15 horses in which telemetric overground endoscopy was performed

Horse details & clinical history	Location	Exercise performed	Tolerance of procedure	Clinical findings with telemetric endoscope	Clinical findings on treadmill
1. TB racehorse, abnormal respiratory noise	Indoor school	10 minutes lunged exercise	Some snorting	PI, intermittent EE and partial ACC (L)	Intermittent EE, partial ACC (L), bilateral VCC & DDSP
2. TB racehorse, poor performance	Indoor school	10 minutes lunged exercise	Snorted once at the start of exercise	No abnormality noted	PI
3. TB general riding, lethargy	Indoor school	15 minutes lunged exercise	Well tolerated	PI	Not performed
4. Eventer, poor performance	Indoor school	10 minutes lunged exercise	Good	No abnormality noted	PI
5. General riding, abnormal respiratory noise	Indoor school	9 minutes lunged exercise	Good	PI	PI and lateral PWC
6. TB racehorse, abnormal inspiratory noise	Indoor school	10 minutes lunged exercise	Occasionally tried to rub head when stationary.	Partial ACC (L) and PI	PI, partial ACC (L) and bilateral VCC from progressing to complete ACC (L)
7. TB racehorse, abnormal respiratory noise in races only	Indoor school	10 minutes lunged exercise	Good	PI	Not performed
8. Eventer, abnormal noise low speeds	Indoor school	10 minutes lunged exercise	Some head shaking and snorting at start of exercise	ACC (L), ADAF and DDSP	Not performed
9. TB racehorse, abnormal respiratory noise	Indoor school	10 minutes lunged exercise	Good	PI observed when mouth open	PI , VCC (L), and collapse of the apex of the left corniculate process

10. TB racehorse, possible abnormal respiratory noise	6 furlong straight inclined gallop and 5 furlong circular track	One gallop, one canter on circular track.	Some head shaking and snorting at the start of exercise	No abnormality noted	Not performed
11. TB racehorse, no abnormal respiratory noise in training but gurgling noise reported in races	6 furlong straight incline gallop	One fast canter, one gallop	Good	PI	Not performed
12. TB racehorse, slight abnormal noise in training, but poor performance and pulling up in races	6 furlong straight incline gallop	One fast canter, one gallop	Good	PI, partial ACC (L) at low speeds, but improved to full abduction during fast exercise.	Not performed
13. TB racehorse, recently purchased, marked abnormal respiratory noise	6 furlong straight inclined gallop	Unfit so one moderate canter, one fast canter	Some snorting at walk	Severe PI obstructing over half of the nasopharynx, particularly on pulling up and slower canter speeds.	Not performed
14. TB racehorse, slight whistle at lower speeds, good racing performance	5 furlong straight inclined gallop	One steady canter and one gallop	Good	Mild ADAF	Not performed
15. TB racehorse, previous ventriculectomy and palatoplasty by thermal cautery. Raced twice since surgery and still performing poorly	5 furlong straight inclined gallop	One steady canter, two gallops	Good	PI at slow canter at end of gallops, no abnormality detected during gallop	Not performed

Key: ACC = arytenoid cartilage collapse, ADAF = axial deviation of the aryepiglottal folds, DDSP = dorsal displacement of the soft palate, EE = epiglottic entrapment, PI = palatal instability, PWC = pharyngeal wall collapse, VCC = vocal cord collapse, L = left



7.8 Endoscopic images taken during overground endoscopy on the gallops (a & b) and during lunged exercise (c & d): (a) complete symmetrical abduction of the arytenoid cartilages (horse 12), (b) severe billowing of the soft palate obscuring much of the nasopharynx (horse 13), (c)) left arytenoid cartilage collapse and dorsal displacement of the soft palate (horse 8), and (d) intermittent epiglottic entrapment (horse 1).

7.4.3 Discussion

This preliminary study has shown that excellent diagnostic images of the URT are achievable in the horse during normal exercising conditions, both on the lunge and during fast ridden exercise.

Endoscopic examination of the URT during field exercise has advantages over the use of a high-speed treadmill. Firstly the exercise test can be conducted in the environment typically used for competition and horses may be examined in a manner appropriate to their discipline. For example, dressage horses can be examined in a collected outline, and racehorses can be examined on the gallops. In addition, the effects of the tack and jockey are accounted for. The time and cost associated with an overground endoscopic examination is likely to be substantially less than that associated with TM endoscopy. Several training sessions are recommended to adequately habituate horses prior to exercise testing on a high-speed treadmill (Sloet van Oldruitenborgh-Oosterbaan and Clayton 1999), where as for this procedure no training sessions were required.

As expected the speeds achieved during lunged exercise were not sufficient for all forms of upper airway collapse to occur. In all cases where lunged exercise was followed by treadmill exercise, additional abnormalities were observed during the faster speed steps on the treadmill that were not observed on the lunge. It is also anticipated that diagnosis of URT collapse on trainers' gallops may not be straight forward in all cases. Whilst it is likely that a diagnosis may be made in horses that readily make abnormal respiratory noise in training, there are a proportion of horses that are reported only to make abnormal noise during racing. There is variation between training yards with respect to the speeds achieved during training (Dyson *et al.* 2004) although 'work' speeds do appear to correspond to average racing speeds. The length of training gallops is also likely to vary. Where only five or six furlong gallops (as described in this study) are available, it is not possible to recreate the race distances encountered during longer flat races and National Hunt (jump) racing. During treadmill exercise it is possible to design standardised exercise tests whereby horses are exercised to near fatigue, thereby improving the chance of making a diagnosis. However such tests are not readily transferable to the field and further work will be necessary in order to design appropriate testing protocols for field use.

In conclusion this study has shown that it is possible to perform endoscopy during over-ground exercise in order to make a diagnosis of URT collapse. Further validation is necessary to compare findings made during TM endoscopy with similar work efforts in the field. However, it is anticipated that in future the use of over-ground endoscopy should enable a greater number of horses to have a diagnosis of dynamic airway obstruction established, thereby improving equine welfare. In addition, the use of such techniques will more readily facilitate clinical research into URT disorders.

7.5 Further clinical use

Further to the preliminary testing, the system has been used in over 250 clinical cases. This system has proved safe for both horse and rider. Although horse injury was not assessed objectively, (as this would require a revisit to all cases the following day to perform a musculoskeletal assessment), there have been no trainer reported injuries to any horse. In addition there have been no horse or rider falls.

However, with any high speed exercise the risk of injury should be considered. It would seem likely that the risk of injury during overground endoscopy would be similar to the risk of injury during training or racing, depending on the intensity of the exercise test used. It has previously been shown that orthopaedic injury is correlated with speed and distance (Parkin 2008). Several studies have reported the incidence of musculoskeletal injury during racing and training (Parkin 2008).

On the basis of the development of a telemetric endoscope at the University of Bristol, there are now several products commercially available. Three other descriptive papers have subsequently been published, which all further confirm the potential benefits of overground endoscopy (Desmaizieres *et al.* 2009; Pollock *et al.* 2009; Pollock and Reardon 2009).

Although overground endoscopy had clearly enabled many more horses to have undergone a dynamic endoscopic examination than would have done previously, it is imperative that further validation of this diagnostic procedure is undertaken.

7.6 *Future technology developments*

The extensive testing of this overground endoscope has highlighted several areas where improvement of the equipment could be made. In many cases mucus on the camera impaired image quality at some point during the endoscopic examination. This may be of less importance in horses exercising sub-maximally when the endoscope can be removed, cleaned and replaced, but for racehorses performing a maximal exercise test if mucus impairs the image such that it is non-diagnostic, the exercise test would need to be repeated on a separate day. Therefore the development of a remote operated air/ water pump would greatly benefit overground endoscopy. In addition, further miniaturisation of the equipment, increased light output and increased telemetry range would be optimal. The addition of a better microphone into the system to enable concurrent recording of respiratory noise with the endoscopy image would also be beneficial. Improvements in battery time or the provision of multiple changeable battery packs would enable a greater number of horses to be assessed on the same day. It was noted that the endoscope is readily moved by airflow/wind whilst the horse is galloping and therefore a brace to support the endoscope was also required. The hand-held control box should ideally incorporate an in-built recorder and have the ability to review the images immediately. In addition, the ability to see the image on the screen in sunlight needs addressing. Improvements in the recorder and camera quality should be undertaken to reduce the image blurring during frame by frame replay. Overall the equipment should be more robust and reliable, as during the testing numerous leads and electronics failed due to the continual vibration of being mounted on a galloping horse.

Some of these suggested changes have now been addressed in newer commercial systems[89] such as multiple battery packs, improved lighting, stiffer insertion tubes and air/water pumps. However, this has come at the cost of miniaturisation with commercial systems weighing approximately 30kg.

One of the advantages of treadmill testing has been the ability to perform measurements of ventilation, airflow, pulmonary mechanics and assessment of gas exchange, either separately or concurrently with dynamic URT endoscopy. It has been suggested that definitive assessment of the presence of respiratory obstruction can be made only by the quantitative determination of upper airway flow mechanics (Kastner *et al.* 1998). Evans (2008) also suggested that quantification of respiratory function in horses with URT obstructions during exercise would assist with decisions concerning treatment and evaluation of response to treatment. A field based system has been developed (COSMED K4b^2), but there have been some concerns as to the accuracy and design of the equipment (Art *et al.* 2006; Lepretre *et al.* 2009) and it is currently not used widely in clinical practice. Further research is required to assess which measure of airflow/ ventilation is most appropriate to determine the effect of an URT obstruction. It would seem appropriate that this could be incorporated into future overground endoscopes.

Chapter 8 Comparisons of overground endoscopy and treadmill endoscopy in U.K. Thoroughbred racehorses

8.1 Introduction

Previous chapters have highlighted that endoscopy during exercise is required to make a definitive diagnosis of dynamic upper respiratory tract obstructions. Over the past 20 years this has been possible by performing endoscopy during treadmill exercise (Morris and Seeherman 1991; Kannegeiter and Dore 1995; Martin *et al.* 2000; Dart *et al.* 2001; Tan *et al.* 2005; Lane *et al.* 2006a), however concerns have been raised as to whether treadmill exercise is representative of racing. Although there are variations in treadmill exercise test protocols, many centres perform an incremental standardised exercise test which often is continued to the point of fatigue (Rose and Hodgson 1994; Jose-Cunilleras *et al.* 2006; Lane *et al.* 2006a; Vincent *et al.* 2006). It has been argued that the incremental test may not be appropriate for a horse exercising over sprint distances of less than a mile and a more representative test for sprinters would be to start the exercise test at close to maximal speeds and maintain this until the horse fatigues (Rose and Hodgson 1994; Parente 1996). Although studies have documented variations between treadmill exercise and field exercise (Barrey *et al.* 1993a and b; Sloet van Oldruitenborgh-Oosterbaan and Barneveld 1995; Courouce *et al.* 1999; Sloet van Oldruitenborgh-Oosterbaan and Clayton 1999; Courouce *et al.* 2000; Evans 2004) it remains unclear to what degree the incremental treadmill exercise test does or does not replicate the work required for thoroughbred racing.

In the previous chapter the feasibility of performing endoscopy during ridden exercise in the field was documented. However further validation of this technique is required. In most circumstances overground endoscopy has been performed at the trainer's premises over routine training speeds and distances. Many U.K. trainers undertake interval training on short inclined gallops and it is likely that the speeds (Dyson *et al.* 2003), distances, inclines, surfaces and number of exercise increments vary widely between trainers. In the U.K., thoroughbred horses race over distances varying from five furlongs (~1000m) up to four and a half miles (~7200m). Therefore it is likely that undertaking overground endoscopy during routine training is also not representative of race conditions.

Further information is required on the validity of both treadmill endoscopy and overground endoscopy, how these two techniques compare with each other and how they compare to race conditions. An ideal study would involve the comparison of treadmill endoscopy and overground endoscopy in the same horses a few days apart. However, it is difficult to recruit thoroughbred racehorses to undergo both procedures. Therefore preliminary information may be obtained from indirect comparisons of treadmill and overground endoscopy. The aim of this study was to report the results of a limited number of horses in which direct comparisons were made and to undertake indirect comparisons of treadmill endoscopy and overground endoscopy.

8.2 Materials and Methods

This study was restricted to thoroughbred racehorses referred for investigation of abnormal respiratory noise and/or poor athletic performance.

Overground endoscopy

For horses with a history of abnormal respiratory noise during training, the endoscopy was performed during a normal 'work' training session. For those that were referred with a history of abnormal noise or poor performance only during races the trainers were asked to perform a strenuous training session. If no abnormality was observed further exercise was undertaken at the trainer's discretion. The speeds, distances and inclines that the exercise test was performed over were recorded using a GPS monitor[10]. The distance was recorded from the start of exercise to the end of exercise, therefore includes the distance for acceleration and deceleration. When more than one interval was performed, the distance of each interval was added to calculate a total distance and this was approximated to the nearest 100m. Heart rates were recorded concurrently throughout the exercise test[10].

Treadmill endoscopy

All horses underwent a standardised incremental exercise test. The test protocol has previously been described (Franklin *et al.* 2002a), but briefly consists of one minute at 6, 8 and 10m/s on a 10% incline, followed by further increments of 1 m/s at one minute intervals. The total distance of the exercise test was recorded and approximated to the nearest 100m. The distance was recorded from the start of the 6m/s speed step to the point were the exercise test ended (i.e. does not include the distance for deceleration). Heart rates were also recorded concurrently throughout the exercise test[11].

Direct comparison

Both procedures were performed in the same horse within ten days of each other.

Indirect comparison

The results of overground endoscopy performed in 50 racehorses was compared to the results obtained during treadmill endoscopy in a further 50 racehorses. Each horse referred for overground endoscopy was randomly matched to a horse referred for treadmill endoscopy within the last three years. Horses were matched for age, gender, use (Flat v National Hunt (NH)) and presenting complaint (abnormal respiratory noise v poor performance).

Racing distances

For horses that had raced previously the distance the horse last raced over was recorded (www.racingpost.co.uk) to permit comparisons with the exercise test.

Data Analysis

Statistical analysis was performed using SPSS 16.0 for Windows. Chi-square test (with Yates continuity correction) or Fisher's exact tests were used to compare the prevalence of dorsal displacement of the soft palate (DDSP), palatal instability (PI), palatal dysfunction (DDSP &/or PI), arytenoid cartilage collapse (ACC), vocal fold collapse (VCC), axial deviation of the aryepiglottic folds (ADAF) and normal upper airway function between the overground endoscopy and treadmill endoscopy groups. Fisher's exact tests were used to compare the diagnosis rate of the two procedures with the presenting complaint. Independent t-tests were used to compare the exercise test distances, peak speed and peak heart rate for overground endoscopy and treadmill endoscopy groups. Independent t-tests were used to compare peak speed for flat and NH during the overground test and during the treadmill test. These statistical analyses were repeated using the McNemar's test and paired t-tests to take into account the initial matching process and there were no differences in the results obtained. Therefore, the statistical methods for analysing unpaired data are presented here because the matching process was used only to ensure comparability of the two groups. A paired t-test was used to compare the exercise test distance with the horse's last race distance for both flat and NH and for both diagnostic procedures. Statistical significance was set at $P<0.05$.

8.3 Results

Direct comparison

Four horses (3 flat, 1 NH) underwent both procedures, the results of which are shown in table 8.1. The time period between the two tests was from two to ten days, and horses continued normal training between the tests. In two horses the overground test was performed first and in two the treadmill test was performed first. In three horses DDSP was observed during treadmill endoscopy but was not observed during overground endoscopy. These horses had a history of abnormal noise during racing and in no case was the presenting complaint reproduced during the overground endoscopy test as abnormal noise was not heard by the veterinary surgeon, trainer or jockey; whereas abnormal noise was heard during the treadmill test when DDSP occurred. In three horses the distance over which overground endoscopy was performed was substantially lower than the distance that horse last raced over. In two flat horses the distance covered during the treadmill exercise test was greater than that in the horse's last race. Heart rates were recorded during both tests in three horses. In one horse similar peak heart rates were reached during both tests, however in two horses the peak heart rate during the overground test was substantially lower than that reached on the treadmill.

Table 8.1 The results of the direct comparison between overground endoscopy and treadmill endoscopy which were both performed in four horses. (Distance in metres rounded to nearest 100m.) For the overground endoscopy, the exercise test was performed over the entire length of the gallops in all cases, and only one increment was performed. DDSP – dorsal displacement of the soft palate, PI – palatal instability, NAD – no abnormality detected.

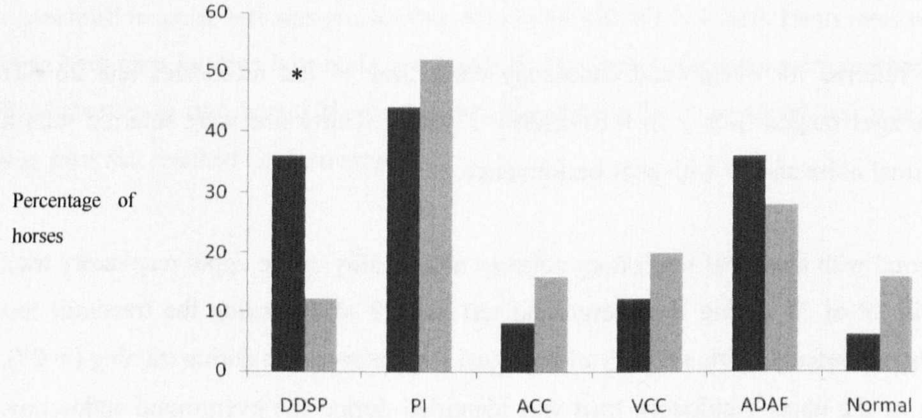
History	Abnormal noise during racing	Abnormal noise during training and races	Poor performance in races	Abnormal noise and poor performance in races
Type	Flat	Flat	NH	Flat
Distance last raced over miles/ furlongs (metres)	1m4f (2400m)	5f (1000m)	2m6½f (4500m)	1m 4f (2400m)
Treadmill				
Peak speed km/h (m/s)	43.2 (12m/s)	36 (10m/s)	43.2 (12m/s)	36 (10m/s)
Distance m	3200	1800	3000	1800
Incline	10%	10%	10%	10%
Peak heart rate bpm	234	233	230	224
Endoscopy result	DDSP	DDSP	PI	DDSP
Overground				
Peak speed km/h	53	60	48	58
Distance m	1000	1400	1400	1000
Incline	4.8%	3.6%	6%	4.8%
Peak heart rate bpm	-	230	211	210
Endoscopy result	PI (mild)	PI (mild)	PI	NAD

Indirect comparison

The 50 horses referred for overground endoscopy comprised 24 flat racehorses and 26 NH racehorses. The ages ranged from 2 to 8 (median = 5 years). Thirty one were referred with a history of abnormal noise and 19 with poor performance.

For horses referred with abnormal respiratory noise an abnormality of the upper respiratory tract was observed in 29 of 31 during the overground test and 29 of 31 during the treadmill test ($p=1.0$). In all horses referred with a history of abnormal respiratory noise during training ($n=27$), an abnormality of the upper respiratory tract was identified during the overground endoscopy. Four horses were referred for overground endoscopy with a history of abnormal noise present only during races, and in only 2 was this noise recreated during the overground test. Of the horses referred for poor racing performance without respiratory noise an abnormality of the upper respiratory tract was observed in only 13 of 19 during the overground endoscopy but was observed in 18 of 19 during the treadmill endoscopy, although this was not statistically significant (p=0.09).

The prevalence of dynamic upper respiratory tract obstructions for the overground endoscopy and treadmill endoscopy groups is shown in figure 8.1. Twenty one horses were diagnosed with complex upper respiratory tract obstructions during overground endoscopy and twenty six were diagnosed with complex upper respiratory tract obstructions during treadmill endoscopy. There was no significant difference in the number of horses found to have normal upper airway function (p=0.20). In addition there were no differences between the two groups in the number diagnosed with dynamic laryngeal collapse; ACC (p=0.34), VCC (p=0.41) and ADAF (p=0.52). When palatal dysfunction was assessed (i.e. presence of either DDSP or PI) there was no significant differences between the two groups (p=0.11). However, when the conditions were assessed separately there was a significant difference in the prevalence of DDSP (p=0.01) which was observed in only 12% of horses undergoing overground endoscopy compared with 36% of horses undergoing treadmill endoscopy. For flat racehorses (n=24 in each group), 2 were diagnosed with DDSP during overground endoscopy and 9 during treadmill endoscopy. For NH racehorses (n=26 in each group), 4 were diagnosed with DDSP during overground endoscopy and 9 during treadmill endoscopy. There was no significant difference in the prevalence of PI (p=0.55).



8.1 The prevalence of upper airway obstructions identified in 50 racehorses assessed by overground endoscopy (grey bars) and 50 assessed by treadmill endoscopy (black bars). DDSP- dorsal displacement of the soft palate, PI- palatal instability, ACC- arytenoid cartilage collapse, VCC- vocal cord collapse, ADAF- axial deviation of the aryepiglottic folds. * denotes a statistically significant difference.

There were significant differences in the overground exercise test protocol compared with the treadmill exercise test protocol (table 8.2). In 44 horses the overground endoscopy was performed on straight inclined training gallops with distances varying from approximately 1000m (5 furlongs) to approximately 2000m (10 furlongs) (median 1400m). Twelve different gallops were used. In 27 cases (18 flat, 9 NH) horses were exercised up the gallops once and in 17 (6 flat, 11 NH) the test was divided into 2 or 3 interval sessions with rest periods in between. In six horses (all NH) the endoscopy was performed on a 2400m (1½ mile) circular course. The treadmill exercise test was performed as a single continuous exercise test in all horses. The total test distance for overground endoscopy varied from 800 to 3600m and for treadmill endoscopy from 1000m to 5000m. There was a significant difference in the exercise test distance between the two groups ($p=0.02$), with the treadmill tests being longer. The treadmill exercise test was performed on a 10% incline, where as the inclines of the gallops varied from 0.6% to 6%. In all cases the peak speed reached was greater during the overground exercise test than during the treadmill exercise test. There was a significant difference ($p=0.02$) in peak speed between flat (mean 58 km/h) and NH horses (mean 55 km/h) during the overground exercise test. There was also a significant difference in peak speed during the treadmill test ($p=0.03$), however NH horses achieved a higher final speed step than flat horses. There was no significant difference in peak heart rate achieved between the treadmill exercise test and the overground exercise test ($p=0.24$). For overground exercise tests there was a significant difference in test distance when the test was performed in more than one interval (mean distance 2600m) compared to tests in which only a single bout of exercise was performed (mean distance 1500m) ($P<0.001$). There was no significant difference in peak speed ($p=0.43$) between single tests and tests performed in more than one interval.

Table 8.2 Comparisons between the overground exercise test parameters and the treadmill exercise test parameters from the indirect study. * denotes a statistically significant difference

	Overground endoscopy test	Treadmill endoscopy test	
Total test distance (m)			
Range	800-3600	1000-5000	
Median	2000	2400	*
Incline (%)			*
Range	0.6-6	10	
Median	3.6	10	
Peak speed (km/h)			
Range	43-66	29-43 (=8-12 m/s)	
Median	56	40	*
Peak heart rate			
Range	195-249	186-234	
Mean	221	218	

Eighty-six horses had raced at the time of examination. The distance last raced over and test distances for flat and NH horses are shown in table 8.3. For flat racehorses there was no significant difference between either the overground test and race distance ($p=0.26$) or treadmill test and race distance ($p=0.53$), although there was a trend for the overground test to be shorter than the race and the treadmill test to be longer. However, for NH horses there was a significant difference between both the overground test and race distance ($p<0.001$) and the treadmill test and race distance ($p<0.001$), where both procedures were performed over shorter distances than that of racing.

Table 8.3 A comparison of the distances of the last race (n=86) versus the distances covered during the exercise test in the indirect comparison for both flat and national hunt racehorses

	Flat	National Hunt
Last race distance (m)		
Range	1000-3400	3200-5400
Median	1600	4200
Total overground test distance (m)		
Range	1000-3200	800-3600
Median	1400	2400
Treadmill test distance (m)		
Range	1000-3300	1000-5000
Median	2100	2550

8.4 Discussion

This study provides preliminary data comparing overground endoscopy and treadmill endoscopy. As previously acknowledged an ideal comparative study would involve both procedures being performed in the same horses a few days apart. It is, however, difficult to recruit horses for such a study and it is likely that considerable funding would be required in order that both procedures may be offered to the trainer free of charge. As a result, only four horses underwent both treadmill endoscopy and overground endoscopy on the trainer's gallops. The results of indirect comparisons may be more susceptible to error compared with the direct comparisons. However, in this study, the results of the direct comparison support the results of the indirect comparison, thus increasing the likelihood that the results are a true finding rather than occurring by chance.

The treadmill and overground endoscopy procedures have to be undertaken in different situations using different tack and endoscopes. However, overground endoscopy enabled a diagnosis of upper airway obstruction in all horses with a history of abnormal noise during training. However, for horses referred with abnormal noise only occurring during racing or for poor racing performance overground endoscopy was less likely to result in a diagnosis of URT collapse than treadmill endoscopy. For horses referred for poor performance with no noise, a sample size calculation revealed that 26 horses in each group would be required to demonstrate a statistically significant difference. The results of both the direct and indirect comparisons suggest that diagnosis of dynamic URT obstructions are dependent on the type of exercise test that is undertaken. In particular there was a significant difference in the proportion of horses that progressed from palatal instability to DDSP. Dorsal displacement of the soft palate was diagnosed more frequently during treadmill endoscopy than during overground endoscopy. However there was no difference in the prevalence of dynamic laryngeal disorders (arytenoid cartilage collapse, vocal fold collapse or axial deviation of the aryepiglottic folds) between the two testing conditions. It is recommended that care should taken when interpreting negative findings during overground endoscopy in horses that only make abnormal respiratory noise during races or that are presented with a history of poor performance without abnormal respiratory noise. Similarly, veterinary surgeons should not discount a diagnosis of PI when overground endoscopy is performed under training conditions as this may progress to DDSP under more strenuous exercise such as during racing or during treadmill endoscopy.

The differences in the prevalence of DDSP between the two techniques are most likely explained by differences in the exercise tests. Although the aetiopathogenesis of DDSP has not been fully elucidated, in many racehorses it is reported to occur at the end of the race and is also observed to occur at the end of the treadmill exercise test (Franklin 2002). This is likely due to fatigue and highlights the importance of undertaking a strenuous exercise test to confirm the diagnosis of DDSP. Those cases in which DDSP occurs readily on the trainers gallops may represent more severely afflicted cases and this should be considered if overground endoscopy is used in clinical research.

The treadmill test appears more strenuous than the tests that were performed overground. Horses undergoing treadmill endoscopy were exercised over longer distances and on higher inclines albeit at lower speeds than were performed overground. It has previously been reported that the effect of gradient on oxygen uptake is substantial (Eaton 1994) and that the effect of increasing gradient on the cost of transport is greater than the effect of increases in speed (Schroter and Marlin 2002). Treadmill exercise testing is also more likely to result in fatigue because of the nature of the test, whereby speed is increased until the horse is no longer able to maintain pace with the treadmill. In addition, because most trainers have short inclined gallops, it was often necessary to perform the overground exercise test in intervals rather than as a continuous test. The rest periods between intervals may allow for partial recovery to occur and may delay the onset of fatigue (Midgley *et al.* 2007). Despite the differences in speeds and distances, during the indirect comparison the peak heart rates reached during both tests were similar, but were likely sustained for a shorter duration in the overground tests. In the direct comparison although similar peak heart rates were reached in one horse, in two horses maximum heart rate was definitely not reached during the overground tests.

For performance testing in human athletes a valid exercise test protocol is one which resembles the performance being tested as closely as possible (Currell and Jeukendrup 2008). Therefore in racehorses the ideal exercise test is one which most closely replicates the work of racing. Runners may also undertake some interval training as part of their training regime; however exercise tests are typically conducted as time trials or time to exhaustion (Currell and Jeukendrup 2008). Performing an exercise test in intervals is unlikely to be appropriate for runners and is used for athletes performing intermittent sports such as football (Bangsbo *et al.* 2008).

It is likely that neither the overground tests nor the treadmill tests undertaken accurately replicate race conditions. The results show that for either treadmill or overground exercise testing, race distances are easier to replicate in flat racehorses than in NH racehorses. Despite this, fewer flat horses were diagnosed with DDSP during overground endoscopy than during treadmill endoscopy. The differences in the prevalence of DDSP may occur as a result of underdiagnosis during overground endoscopy or overdiagnosis during treadmill endoscopy. Although the possibility of overdiagnosis of DDSP should be considered on the treadmill, because of the potential for longer test distances than race distances, this seems unlikely from the results of the direct comparison. In all 3 flat racehorses referred for abnormal respiratory noise during racing that were examined under both conditions the presenting complaint was not replicated during the overground endoscopy but was replicated during treadmill endoscopy whereby DDSP was confirmed. It is possible that if neither test accurately replicates racing conditions the prevalence of DDSP may be in fact be underestimated by both methods, albeit to a greater degree during overground endoscopy on the training gallops than during treadmill endoscopy. The use of inclined exercise in training means that average training speeds are less than average race speeds. Inclined exercise is used in both training and testing to increase work effort without increasing speed, thereby reducing the risk of musculoskeletal injury (Evans 1994). However, inspiratory pressures become more negative at higher speeds (Ducharme *et al.* 1994), and it is unclear whether horses tested at slower speeds on an incline experience the same inspiratory pressures that occur when exercising at faster speeds during a race. This may explain the difficulties in re-creating the presenting complaint in some horses.

When recreating race distances it should also be considered that the distances for racing and treadmill used in this study did not include the distance required for the horse to pull up, whereas when horses were exercised on the trainers gallops the peak speed usually occurred mid way along the gallops and speeds slowed in the latter part of the test allowing the horse to pull up gradually before reaching the end. Ideally gallops should be longer than the race distance and not on a steep incline if racing speeds are to be recreated. The average speed of the exercise test, rather than the peak speed, could more readily be compared with the average speed during a race, thereby confirming that an appropriate test has been performed. Despite this, trainers are often reluctant for horses to perform strenuous tests, and the risk of injury should be considered. Further work is required to understand the work efforts involved in various races and how these compare with exercise tests that are currently being used both on the treadmill and in the field.

For overground endoscopy further study is required to establish how valid or reliable it is to perform an exercise test in intervals. A more accurate test for overground endoscopy may necessitate a circular or racecourse gallop.

In conclusion, the results of both the direct and indirect comparisons suggest that DDSP is diagnosed less often during overground endoscopy than during treadmill endoscopy. Overground endoscopy performed on the trainer's gallops is of greatest diagnostic value if abnormal respiratory noise is made during routine training. In horses that only make abnormal noise during races, or are reported to have poor race performance without abnormal noise, it is recommended that efforts are made to recreate the conditions encountered during racing (e.g. with circular gallops or at a racetrack) which may be significantly different to those encountered during training. Furthermore care should be taken in interpreting negative findings if racing conditions have not been appropriately replicated. Strenuous exercise tests may be more easily performed on a treadmill, on a circular gallops or at a racetrack than by performing multiple exercise intervals in the field. It is unlikely that one method should be considered 'better' or 'gold standard' compared to the other. Both techniques have advantages and disadvantages and the diagnostic value of either technique lies in the appropriateness of the exercise test to race conditions for each individual horse.

Chapter 9 Assessment of the exercise tests used during overground endoscopy in U.K. thoroughbred racehorses and how these may affect the diagnosis of dynamic upper respiratory tract obstructions

9.1 Introduction

Overground endoscopy is being performed with increasing frequency in the UK. Previous chapters comparing overground endoscopy and treadmill endoscopy suggested that the type of exercise test may affect the ability to make a diagnosis of dynamic URT obstructions. In particular, the occurrence of dorsal displacement of the soft palate, was more likely to occur under more strenuous exercise testing conditions. In many circumstances overground endoscopy is performed at the trainer's premises over routine training speeds and distances. However, in contrast to racing in some other countries, many U.K. trainers only undertake training on short inclined gallops, therefore the speeds and distances experienced during training may not be the same as those experienced during racing.

The successful clinical application of overground endoscopy systems requires the development of appropriate field exercise testing protocols. The aim of this study was to report the exercise test parameters used during overground endoscopy in UK thoroughbred racehorses and to investigate potential effects of these on the diagnosis of URT obstructions.

9.2 Materials and Methods

This study was restricted to thoroughbred racehorses referred for overground endoscopy for the investigation of abnormal respiratory noise and/or poor athletic performance. The fifty horses included in chapter 8 were also included in this chapter. Only horses in which the overground endoscopy was performed on a gallops or a racecourse were included. The technique and equipment used was described in the previous chapters. The history and presenting complaints were recorded. For horses with a history of abnormal respiratory noise during training, the endoscopy was performed during a normal gallop training session. For those that were referred with a history of abnormal noise or only poor performance during races the trainers were also asked to perform a strenuous training session. If no abnormality was observed further exercise was undertaken at the trainer's discretion. The speeds, distances and inclines that the exercise test was performed over were recorded using a GPS monitor[10]. The distance was recorded from the start of exercise to the end of exercise and therefore includes the distance for acceleration and deceleration. When more than one interval was performed, the distance of each interval was added to calculate a total distance and this was approximated to the nearest 100m. The average speed of the exercise test was calculated by dividing the exercise test distance with the time taken. Heart rates were recorded concurrently throughout the exercise test[10]. After the exercise test the author assessed whether the presenting complaint had likely been reproduced during the exercise test, taking account of information from the trainer and jockey.

For horses that had raced previously the distance the horse last raced over was recorded (www.racingpost.co.uk) to permit comparisons with the exercise test. In addition, the average speed for the race was calculated by the time taken by the winning horse to complete the race. A test race ratio was calculated, whereby the total exercise test distance was divided by the distance the horse last raced over. Therefore, horses undergoing exercise tests at equal or greater distances than the horses racing distance had values greater than or equal to one. Where available, the actual time taken for the horse to complete the race was obtained (www.turftrax.com).

Statistical analysis

Statistical analysis was performed using PASW 17.0. Preliminary statistics were undertaken to establish whether data were normally distributed. Non parametric tests were used for skewed data. Horses were divided into three groups according to presenting complaint: abnormal noise in training, abnormal noise in racing and poor race performance without abnormal noise. Chi-square tests were used to compare the presence of URT abnormalities or whether the presenting complaint had been reproduced between the three groups. Spearman or Pearson correlations were used to assess correlations between individual exercise test parameters. Independent t-tests or Mann Whitney tests were used to assess exercise test parameters and the presence of URT obstructions. Wilcoxan signed rank tests were used to compare the test and race data. Statistical significance was set at $P<0.05$.

9.3 Results

The inclusion criteria were met by 140 horses, 80 flat and 60 National Hunt (NH) racehorses. The ages ranged from 2 to 11 years (median 4 years). There were 19 mares, 51 colts and 70 geldings.

The exercise test parameters used are shown in table 9.1. Thirty five different tracks were used. The total exercise test distance varied from 800 to 6100m (median 1900m). The test was performed in more than one increment in 50 horses. The exercise test was performed on a circular/ oval gallops or racetrack in 19 horses. The straight gallops were all inclined to varying degrees, where as the circular gallops used were flat ($p<0.001$). The median test distance undertaken on circular gallops was 3200m, and the median test distance on straight gallops was 1600m ($p<0.001$). There was no significant difference in mean peak speed between circular gallops (57 km/h) and straight gallops (56 km/h) ($p=0.46$). For straight gallops, peak speed was negatively correlated with incline ($R=-.266$ $p<0.001$). There was also a negative correlation between incline and distance ($R=-.403$ $p<0.001$), as inclined gallops tended to be shorter.

Table 9.1 The exercise test parameters used during the overground endoscopy procedure in 140 thoroughbred racehorses

Exercise test parameter	Range	Mean	Median
Total test distance (m)	800 - 6100	2100	1900
Distance of first or only increment (m)	800 - 6100	1700	1400
Peak speed (km/h)	37 - 69	56	56
Average speed (km/h)	29 - 54	40	40
Incline (%)	0 - 10	3	3

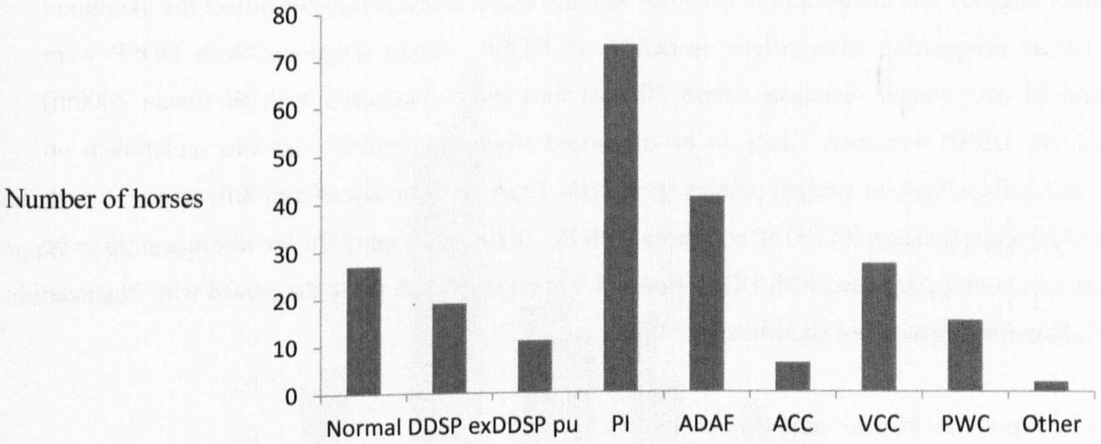
One hundred and twenty five horses had raced prior to the endoscopic examination. For flat racehorses there was no significant difference between median test distance (1600m) and median race distance (1600m) ($p=0.44$). However for NH racehorses median test distance (2500m) was significantly lower than race distance (4200m) ($p<0.001$). There was a significant difference between peak speed achieved by flat horses (58km/h) compared with NH horses (53km/h) ($p<0.001$). The average speeds of the exercise tests for both flat and NH horses were significantly lower than the average speeds needed to win the race ($p<0.001$). Table 9.2 shows the average race speeds for the winning horse for different race lengths, and the peak and average speeds for the exercise test for that category. Average speeds of the exercise test were also significantly slower than the average speed the horse completed the last race ($p<0.001$).

Table 9.2 The winning speeds for the last race prior to referral for overground endoscopy and comparisons with the speeds encountered during the exercise test

Race distance miles/furlongs	Average racing speed km/h	Peak test speed km/h	Average test speed km/h
Flat up to 1mile (=1609m)	54 - 63 (mean 58)	50 – 69 (mean 59)	30 – 50 (mean 41)
Flat greater than 1 mile	53 - 60 (mean 56)	50 – 64 (mean 57)	32 – 47 (mean 41)
NH up to 2 ½ miles (=4022m)	45 - 55 (mean 50)	45 – 66 (mean 55)	32 – 50 (mean 39)
NH greater than 2 ½ miles	44 - 52 (mean 48)	37 – 61 (mean 53)	30 – 54 (mean 41)

The peak heart rates achieved during the exercise tests varied from 178 to 258 bpm (median 219 bpm, mean 220 bpm). In many horses high heart rates were observed prior to exercise and only 8 horses had peak heart rates less than 200 bpm. Five horses were considered to have an abnormally elevated heart rate response during exercise (>250 bpm), of which two horses were confirmed to have paroxysmal atrial fibrillation.

The URT abnormalities identified and the numbers of horses observed with each abnormality are shown in figure 9.1. Normal URT function was observed in 27 horses, a single URT abnormality in 48 and multiple abnormalities in 65 horses. Palatal dysfunction was the most common abnormality observed in 103 horses; 84 had palatal instability during exercise, of which 11 experienced DDSP on pulling up, and 19 had DDSP during strenuous exercise. Axial deviation of the aryepiglottic folds was also observed commonly and there was a significant association with palatal dysfunction ($p=0.001$).



9.1 The endoscopic observations in 140 racehorses undergoing overground endoscopy. Sixty five horses had more than one abnormality observed. DDSP ex – dorsal displacement of the soft palate observed during exercise, DDSP pu – dorsal displacement of the soft palate occurred as the horse pulled up after exercise, PI – palatal instability, ADAF – axial deviation of the aryepiglottic folds, ACC – arytenoid cartilage collapse, VCC – vocal cord collapse, PWC – pharyngeal wall collapse.

There were no significant differences in exercise test parameters between horses with and without a diagnosis of URT obstruction. The median exercise test distance was 1900m ($p=0.84$) and median incline 3% ($p=0.33$) for both groups. The mean speed was 56km/h for horses diagnosed with an URT obstruction and 55km/h for horses without a URT obstruction ($p=0.64$).

Horses reported to make abnormal noise in training

Sixty five horses were reported to make abnormal noise in training. In sixty (92%) horses one or more abnormalities of the URT were observed (figure 9.2). The presenting complaint was reproduced in 53 (82%) horses. Further details of the 12 horses where the presenting complaint was not reproduced are shown in table 9.3.

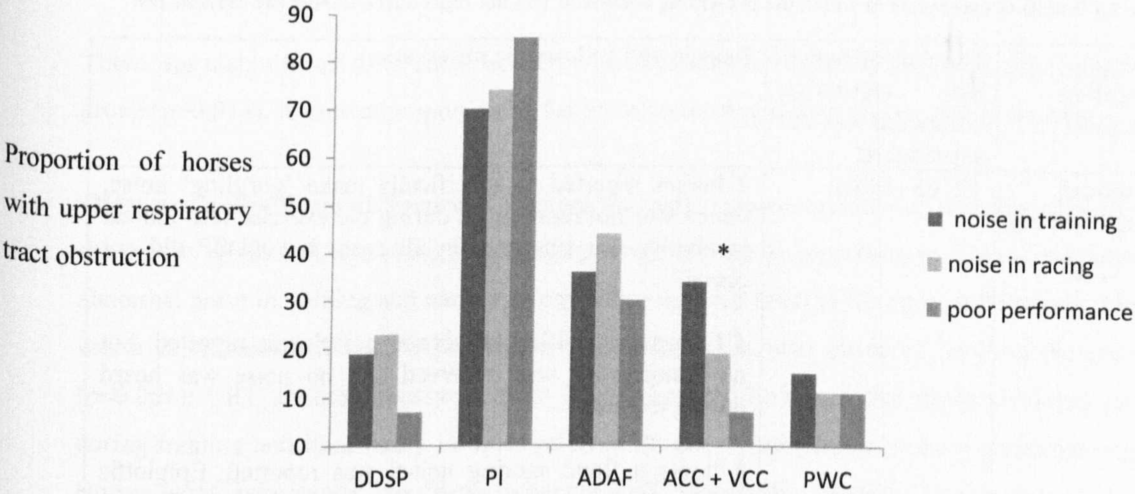
Horses reported to make abnormal noise in racing only

Thirty one horses were reported to make abnormal noise during racing. In 26 (84%) horses one or more abnormalities of the URT were observed (figure 9.2). The presenting complaint was reproduced in 19 (61%) horses. Further details of the 12 horses where the presenting complaint was not reproduced are shown in table 9.3.

Further analysis was undertaken to establish whether exercise test parameters affect the likelihood of horses progressing from palatal instability to DDSP. Horses diagnosed with DDSP were exercised over longer distances (mean 3000m) than those diagnosed with PI (mean 2000m) ($p=0.04$). DDSP was more likely to be diagnosed when the exercise test was undertaken on circular gallops than on straight gallops ($p=0.016$). There were no significant differences in peak speed between horses with DDSP and those with PI. There was a trend for the test race ratio to be greater in horses diagnosed with DDSP (mean 0.9) compared with those diagnosed with PI (mean 0.7), however this was not significant ($P=0.29$).

Horses reported with poor performance and no noise

Forty four horses presented with poor racing performance with no abnormal noise reported by the trainer. Twenty horses were referred for poor or disappointing race performance, 16 for pulling up or stopping, and 5 for slowing, fading or failing to finish. In 27 (61%) horses an abnormality of the URT was observed (figure 9.2). It was difficult to reproduce the presenting complaint for horses in this category (table 9.3). In the three horses (7%) where the complaint was considered to have been reproduced, 2 were reported to have excessive blowing post exercise as well as poor performance and 1 was reported to have become wobbly and to have EIPH as well as racing poorly. In all three cases a non URT reason for the poor performance was identified.



9.2 The proportion of horses with each URT abnormality depending on the presenting complaint. DDSP – dorsal displacement of the soft palate observed during exercise, PI – palatal instability, ADAF – axial deviation of the aryepiglottic folds, ACC+VCC – arytenoid cartilage collapse and / or vocal cord collapse, PWC – pharyngeal wall collapse. * denotes statistically significant difference.

Table 9.3 Details of racehorses in which the presenting complaint was not reproduced during the exercise test

Category of presenting complaint	Number of horses that presenting complaint was not reproduced	Reason and endoscopic observation
Abnormal noise during training	12/ 65 (18%)	7 horses reported to specifically make 'gurgling' noise, which was not reproduced during the exercise test. Palatal instability was observed in all cases but DDSP did not occur. 4 horses unspecified 'abnormal noise' was reported, but no abnormality was observed and no noise was heard during the test. 1 horse a 'loud snoring noise' was reported. Epiglottic retroversion was observed in this horse during walk, but did not occur during faster speeds and only a 'whistle' was heard at faster speeds which was associated with vocal cord collapse.
Abnormal noise during racing	12/ 31 (39%)	7 horses were reported to make unspecified 'abnormal noise', yet no noise was heard during the test. In 5 no endoscopic abnormalities were observed and in 2 only mild palatal instability was observed. 3 horses, a 'gurgling' noise was reported which was not reproduced during the test. 2 showed palatal instability and in 1 horse no abnormality was observed. 2 horses were reported to make abnormal noise concurrently when the horse stopped abruptly in a race, but during the test only a low grade inspiratory noise was heard however both horses performed well and this noise was not associated with stopping suddenly.
Poor performance with no abnormal noise	41/44 (93%)	For horses referred for poor race performance, pulling up in races, stopping in races and slowing suddenly in races this was difficult to reproduce during testing.

Between group comparisons

There was a significant difference between type of racehorse (flat/NH) and presenting complaint group ($p=0.014$). A greater proportion of flat horses were reported to make noise in training.

There was a significant difference in whether the presenting complaint was reproduced between the groups ($p<0.001$), the presenting complaint was easiest to reproduce in horses referred for abnormal noise in training and hardest to reproduce in those referred for poor performance. There was a significant difference in whether a URT abnormality was observed between the groups ($p<0.001$); URT abnormalities were most likely observed in horses that made abnormal noise during training and least likely in those referred for poor performance without abnormal noise. Horses were significantly less likely to have a URT abnormality observed during the test if the presenting complaint was not reproduced ($p<0.001$).

There were no significant differences between the groups in the proportion of horses with dorsal displacement of the soft palate (DDSP) ($p=0.31$), palatal instability (PI) ($p=0.30$), axial deviation of the aryepiglottic folds (ADAF) ($p=0.52$) or pharyngeal wall collapse (PWC) ($p=0.81$) (figure 9.2). There was a significant difference for arytenoid cartilage collapse and vocal fold collapse (ACC+VCC) ($p=0.021$), which was less common in horses referred for poor performance without abnormal noise.

9.4 Discussion

The aim of this study was to report the exercise test parameters used during overground endoscopy in UK thoroughbred racehorses and to identify whether these affected the ability to diagnose URT abnormalities.

The results of this study show there was marked variation in the exercise test parameters that were used during overground endoscopy. The exercise test was most frequently performed at the trainers' premises, therefore tests were highly dependent on the facilities available at that training yard and are therefore very difficult to standardise. The advantages of undertaking exercise tests on high-speed treadmills are that the speeds, distances and inclines can be standardised between horses and as they can be decided upon prior to the test are under exact control of the veterinary surgeon. Whereas during overground endoscopy the exercise tests were more dependent upon the trainer, jockey and facilities, and the veterinary surgeon was less able to specify exact parameters of the exercise test.

For many horses a normal 'gallop' training session was performed, and this type of field exercise test was used in thoroughbreds in two recent publications (Gramkow and Evans 2006; Vermeulen and Evans 2006). However, it has previously been shown that gallop speeds vary considerably between trainers (Dyson *et al.* 2003). Peak speeds during testing were similar to the average speeds obtained from winning horses during racing. However these were maintained only briefly during the exercise test and hence average speeds during testing were significantly lower. For flat horses, the distances performed during training may be similar to race distances; where as for NH horses training distances are markedly shorter than the distances encountered during racing. Interestingly this probably explains why a significantly larger proportion of flat horses were referred for abnormal noise in training compared with NH horses. The differences in the training and racing distance explain why NH horses were often referred for abnormal noise in racing that was not present during training.

In contrast to racing in other countries, many U.K. trainers often only train on short inclined gallops. In exercise test studies from other countries, horses are often trained at racetracks (Davie and Evans 2000; Vermeulen and Evans 2006) or on oval training tracks (Courouce *et al.* 1999; Lindner 2009). It has previously been shown that undertaking similar exercise tests on different oval tracks did not result in differences in physiological or locomotor responses between the two tracks (Courouce *et al.* 1999). It is likely that exercise tests similar to the demands of racing are more likely to be replicated on oval training gallops than on short inclined straight gallops, particularly for NH horses and also for flat horses that race over longer distances. When only short gallops were available it was often necessary to perform the exercise test in intervals. However, the rest periods between intervals may allow for partial recovery to occur and may delay the onset of fatigue (Midgley *et al.* 2007). This study suggests that in many cases undertaking exercise tests at trainer's premises is unlikely to be a valid test of racing.

The heart rate response to exercise was often of limited use in determining whether the exercise test was sufficiently strenuous because it may be influenced by other factors including underlying fitness, excitement, the presence of the endoscope, and also by the underlying disorder causing the poor performance (Courouce *et al.* 1999). High heart rates were readily achieved irrespective of the exercise test parameters.

There were no significant differences in exercise test parameters between horses with and without a diagnosis of URT obstruction. It is likely that URT collapse occurs when a combination of critical negative airway pressure is reached and when fatigue of the upper airway dilator muscles occurs. The finding that similar obstructions were observed irrespective of whether horses were referred for abnormal noise in training or abnormal noise in racing suggests between horse variations may be very important. For example, the inspiratory pressures and degree of fatigue required to induce an URT obstruction in one horse may be different than those required to induce the same abnormality in another horse.

Similar to other treadmill and overground endoscopy studies, palatal dysfunction was the most common URT abnormality observed (Morris and Seeherman 1991; Kannegieter and Dore 1995; Martin *et al.* 2000; Franklin *et al.* 2006; Lane *et al.* 2006a; Desmaizieres *et al.* 2009; Pollock *et al.* 2009). However, similar to the previous chapter, although palatal instability was frequently observed, DDSP was diagnosed less frequently than expected. In this study DDSP was observed in only 20% of horses (14% during exercise, 6% on pulling up), in contrast to 40% of cases in a review of thoroughbred racehorses referred for treadmill endoscopy to the same centre (Lane *et al.* 2006a). For horses referred with abnormal noise in racing it was found that DDSP was more likely if longer distances were performed, which may necessitate a circular or racecourse gallop. As peak speeds were similar for circular and straight gallops, this suggests that DDSP more likely occurs as a result of fatigue (i.e. further distances) than by more negative inspiratory pressures (i.e. faster speeds). There were a high proportion of horses observed to have PI in the poorly performing group. Palatal instability is often associated with abnormal inspiratory noise (Lane *et al.* 2006b). However, this is quieter than the noises associated with other forms of URT collapse (Franklin 2002) and hence may not always be detected by the jockey or trainer. Further understanding of the importance of PI and its effects on airflow and performance are required. In addition, understanding whether it is possible to predict which horses observed to have PI would experience DDSP under more strenuous conditions such as racing would be beneficial.

The differences in the proportion of horses observed to have a URT abnormality when referred for abnormal noise compared to those referred for poor performance without a history of abnormal noise was not surprising. If abnormal noise is present some form of collapse or turbulence within the respiratory tract must exist to create this. It was more difficult to assess horses referred for poor racing performance without abnormal noise. If normal upper respiratory tract function was observed this could either be because the exercise test had not reproduced the URT problem, or that the URT was normal and there was another cause of the poor performance. It was difficult to reproduce the presenting complaint in horses referred for poor race performance. For the majority of horses referred for pulling up, stopping or slowing suddenly in races, this was not reproduced during the exercise test. For horses with poor or disappointing race performances this was either not reproduced, i.e. the horse worked well during the test or was unanswered due to the subjective nature of assessing individual horse's performance. This study confirmed that care should be taken interpreting a normal airway if the presenting complaint was not reproduced during the exercise test.

In conclusion, it is difficult to standardise exercise tests in the field when multiple premises are used and when training gallops differ markedly to racecourses. It was not possible to establish exercise test protocols which should be used for all thoroughbred racehorses. Overground endoscopy performed at a trainer's premises is appropriate for investigation of abnormal noise during training, irrespective of the type of racing performed. For horses that only show clinical signs during racing, the exercise test must be representative of racing in order to establish a definitive diagnosis. This study suggests that undertaking exercise tests over race distances is a key factor. For many horses which race over longer distances this will require the use of a circular gallops (e.g. racecourse) if only short gallops are available at the trainer's premises. Until it becomes possible to standardise field exercise tests better, overground exercise tests should be tailored for each individual horse, particularly taking into account the presenting complaint and the race distance for that horse.

Chapter 10 Characteristics of palatal instability in thoroughbred racehorses

10.1 Introduction

Palatal dysfunction comprises palatal instability (PI) which may or may not progress to dorsal displacement of the soft palate (DDSP). Palatal instability has been described as dorso-ventral billowing movements of the caudal portion of the soft palate, with flattening of the epiglottis against the dorsal surface of the soft palate (Kannegeiter and Dore 1995; Tan *et al.* 2005; Lane *et al.* 2006a). Dorsal displacement of the soft palate occurs when the caudal border of the soft palate becomes displaced to a position above the epiglottis resulting in obstruction of the rima glottidis (Parente *et al.* 2002; Franklin *et al.* 2004; Lane *et al.* 2006a). Observation of DDSP is straight forward, i.e. it is an all or nothing event; where as observation of PI is subjective and interpretation may vary between clinicians.

Ahern (1999a) first described the caudal soft palate conformation and suggested the occurrence of an oropalatal seal (OPS) which assists in maintenance of ventral positioning of the soft palate. Two different contours of the caudal soft palate were described. Firstly, a concave trough in the caudal soft palate was thought to suggest intimate contact of the ventral soft palate with the mucosa of the glossoepiglottic region. In these cases it was also noted that the major part of the epiglottic apex sits above the soft palate and as it curls ventrally the tip of the epiglottis touches the soft palate (Ahern 1999a). The second description was when the caudal soft palate has a convex appearance and the epiglottis lies in contact with the soft palate. Ahern (1999a) suggested that the first mentioned contour could only be explained by the existence of the oropalatal seal, as intrinsic and extrinsic palatine muscular activity alone would be unlikely to produce and maintain this contour. The second mentioned contour was thought to occur when air was able to enter the oropharynx. Furthermore it was suggested that DDSP could only occur following disruption of the OPS.

Some studies have suggested that palatal instability always pre-exists the development of DDSP (Lane *et al.* 2006a), where as others have suggested that DDSP may occur in the absence of PI (Barakzai and Hawkes 2010). It is unclear whether these differences are true reflections of differing pathogenesis between horses or whether they occur because of different endoscope positions or different interpretations by clinicians.

It is acknowledged that horses with palatal instability do not always experience DDSP during the exercise test (Kannegieter and Dore 1995; Lane *et al.* 2006a; Cheetham *et al.* 2008). Previous chapters have shown that a diagnosis of DDSP is dependent on performing a sufficiently strenuous exercise test. However, it is unclear whether it is possible to predict which horses with PI might progress to DDSP if the exercise test was more strenuous or under different circumstances, such as during competition. This might be clinically useful with the increasing use of overground endoscopy in the UK, whereby exercise tests performed at training premises are unlikely to replicate the demands of racing.

Furthermore, it is unclear what degree of stability of the soft palate should constitute 'normal'. Therefore the aim of this study was to attempt to characterise palatal instability more objectively and to assess progression of PI to DDSP.

10.2 Materials and Methods

All thoroughbred racehorses referred for high speed treadmill endoscopy within a 3 year period (2005-2008), in which a diagnosis of palatal instability, dorsal displacement of the soft palate or normal upper airway function were assessed for inclusion. Horses with concurrent axial deviation of the aryepiglottic folds (ADAF) were permitted but horses with a diagnosis of arytenoid cartilage collapse, vocal cord collapse, pharyngeal wall collapse or another upper airway obstruction were excluded. Horses in which a standardised incremental exercise test (Lane *et al.* 2006a) was not performed were excluded. Recordings in which no soft palate was visible rostral to the tip of the epiglottis were also excluded, as assessment would not be possible.

The exercise test consisted of one minute at 6, 8 and 10m/s on a 10% incline, followed by further increments of 1 m/s at one minute intervals. Endoscopic observations were assessed over the last ten seconds of the exercise test or the last ten seconds prior to DDSP. The degree of axial deviation of the aryepiglottic folds, the conformation of the epiglottis, the conformation of the soft palate and the amount the rima glottidis was obscured by the soft palate were assessed according to the following criteria. All videos were assessed in slow motion and frame by frame and grades were assigned when the obstruction appeared most severe.

Axial deviation of the aryepiglottic folds

Graded as none, mild, moderate or severe using the criteria suggested by King *et al.* (2001). Mild ADAF was defined as axial collapse of the aryepiglottic folds, however the folds remain abaxial to the vocal cords. Moderate ADAF was defined as axial deviation of the aryepiglottic folds less than halfway between the vocal cord and midline, whereas severe ADAF was defined as collapse of the aryepiglottic folds more than halfway between the vocal cord and midline.

Epiglottic conformation

Epiglottic conformation was categorised into 3 groups:

1) Convex epiglottic appearance - was defined when the epiglottis maintained a convex shape during exercise, typically only the tip of the epiglottis is in contact with the soft palate (figure 10.1).

2) Flattened epiglottis - described the appearance where the epiglottis loses its convex shape and appears to lie flat or slightly concave on the surface of the soft palate, but the tip of the epiglottis remains ventral to the base (figure 10.2).

3) Tipped up appearance - was assigned when the epiglottis had a flattened or concave appearance and during inspiration the tip of the epiglottis is at the same level or higher than the base of the epiglottis (figure 10.3).

10.1 Convex epiglottic appearance

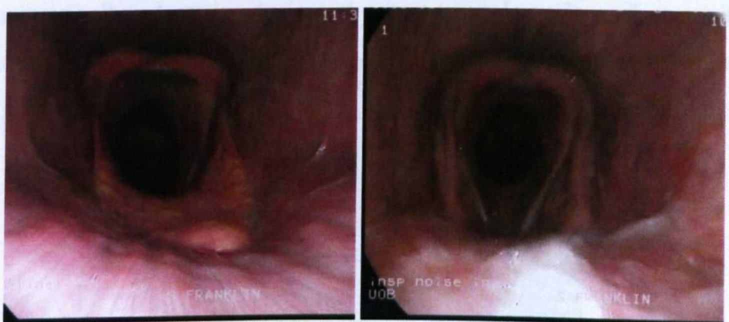
10.2 Flattened epiglottis

10.3 Tipped up appearance of the epiglottis

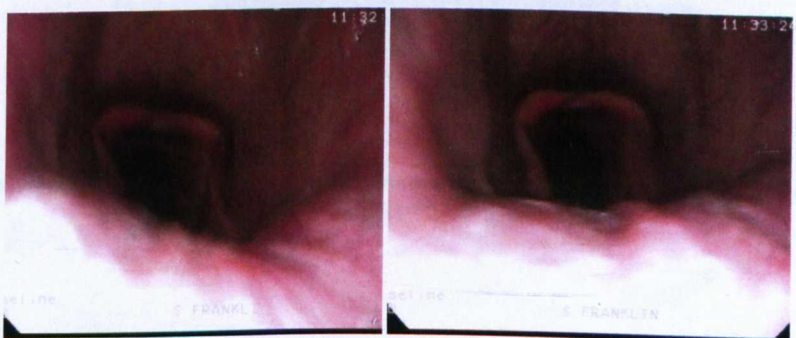
Obstruction of the rima glottidis by the soft palate

The stability of the soft palate was graded as to whether the rima glottidis was obscured by the billowing soft palate. The soft palate was considered stable when no movement or lifting of the soft palate was observed (figure 10.4). Palatal instability with no rima glottidis obstruction was assigned when the soft palate lifts up to the level of the base of epiglottis but the rima glottidis is not obscured (figure 10.5). Palatal instability with rima glottidis obstruction was assigned when the soft palate lifts so that the rima glottidis becomes obscured (figure 10.6).

10.4 Stable soft palate



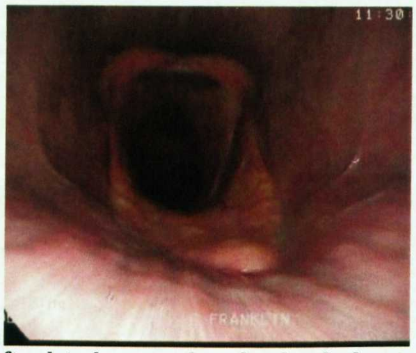
10.5 Palatal instability with no rima glottidis obstruction



10.6 Palatal instability with rima glottidis obstruction

Soft palate conformation

The soft palate of horses with palatal instability was described as either flaccid, billowing dorsally either side of the epiglottis, or billowing dorsally in front of the epiglottis (figures 10.7, 10.8 and 10.9). It was also noted if horses had a sling appearance to the ventrolateral pharyngeal walls at the level of the guttural pouch ostia (figure 10.10). The caudal soft palate of all horses was assessed as to whether concave depressions were present either side of the palatinus muscle. The depressions were subjectively graded as absent, small or large and were graded on inspiration and expiration (figures 10.11, 10.12 and 10.13). Large depressions were assigned when the appearance was similar to that described by Ahern (1999a), whereby concave troughs were present across the width of the soft palate either side of the palatinus muscle (figure 10.11). A small depression was assigned when an area of the caudal soft palate maintained a concavity, however this did not extend from the palatinus to the lateral pharyngeal wall (figure 10.12). Caudal movement of the larynx was used to determine inspiration as described by Tsukroff *et al.* (1998). Subsequently still images were obtained from all horses when the depression appeared at its greatest. The distance from the palatinus to the lateral pharyngeal wall was measured and the width of the concave depression was measured[12]. The relative size of the depression to the distance from the midline to the lateral pharyngeal wall was then calculated (figure 10.11 and 10.12).

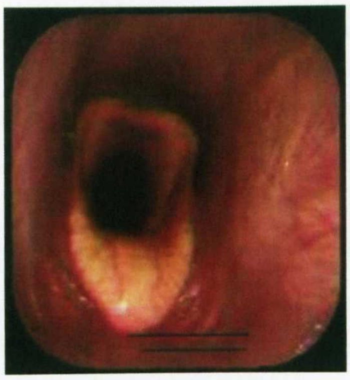


10.7 Flaccid appearance of the soft palate, however the soft palate had no tendency to billow further into the airway

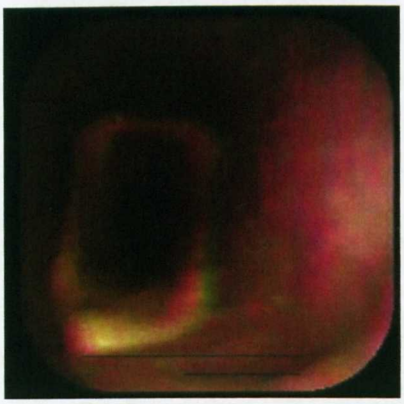
10.8 Billowing of the soft palate either side of the epiglottis

10.9 Billowing of the soft palate in front of the epiglottis

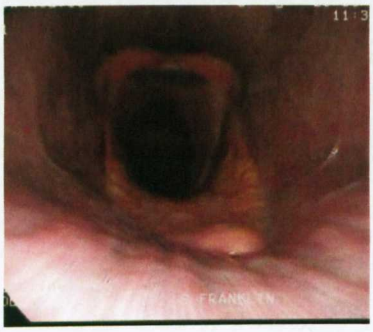
10.10 Sling appearance of the ventrolateral pharyngeal walls



10.11 Large depression in the caudal soft palate (by subjective grading). This measured 85%.



10.12 Small depression in caudal soft palate (by subjective grading). This measured 52%.



10.13 No depression visible in the caudal soft palate

In all horses the soft palate stability, epiglottic conformation and axial deviation of the aryepiglottic folds was graded separately by two people, and twice by the same person to assess inter and intra-observer repeatability and reliability.

Statistical analysis

Statistical analysis was performed using PASW 17 for Windows. Fisher's exact tests were used to identify any associations between endoscopic characteristics and diagnosis (normal, palatal instability that did not progress to DDSP and palatal instability that did progress to DDSP). Fisher's exact tests were used to identify associations between endoscopic characteristics. Fisher's exact tests were used to identify which endoscopic characteristics were associated with progression of PI to DDSP. An independent T-test used to compare the mean size of depression in horses that displaced with those that did not. Kappa measure of agreement was used to assess inter & intra-observer reliability of the observations. Statistical significance was set at $P<0.05$.

10.3 Results

The endoscopic observations of 74 horses were included in this study. Seven horses had no evidence of palatal instability and were considered to have normal soft palate function, 36 had palatal instability which did not progress to DDSP, and 31 had PI which did progress to DDSP.

Intra observer reliability showed very good agreement for stability of the soft palate ($\kappa=0.91$) and epiglottic conformation ($\kappa=0.89$), and good agreement for axial deviation of the aryepiglottic folds ($\kappa=0.72$). Inter observer agreement showed good agreement for stability of the soft palate ($\kappa=0.77$) and epiglottic conformation ($\kappa=0.72$) and moderate agreement for axial deviation of the aryepiglottic folds ($\kappa=0.61$).

There were significant associations between the three diagnostic categories and the stability of the soft palate, epiglottic conformation and axial deviation of the aryepiglottic folds (table 10.1).

Table 10.1 The prevalence of endoscopic characteristics observed in 74 horses

Characteristic	Number of horses			P value
	Normal palate function	PI that did not progress to DDSP	PI that progressed to DDSP	
Stability of the soft palate				
Stable	7	0	0	<0.001
PI with no rima glottidis obstruction	0	24	12	
PI with rima glottidis obstruction	0	12	19	
Epiglottic conformation				
Convex	7	2	0	<0.001
Flat	0	14	4	
Tipped up	0	20	27	
Axial deviation of the aryepiglottic folds				
None	6	5	5	0.002
Mild	1	25	14	
Moderate	0	4	10	
Severe	0	2	2	

The stability of the soft palate was significantly associated with epiglottic conformation ($p<0.001$) and severity of ADAF ($p<0.001$). Severity of ADAF was associated with epiglottic conformation ($p<0.001$). Whereby, all horses with severe ADAF had also had a tipped up epiglottic appearance and 86% of horses with moderate ADAF had a tipped up epiglottic appearance.

There were significant associations between the three diagnostic categories and the presence of concave depressions in the caudal soft palate, a sling appearance and billowing in front of the epiglottis (table 10.2).

Table 10.2 The prevalence of endoscopic characteristics of the caudal soft palate in 74 horses

	Number of horses			
Characteristic of soft palate conformation	**Normal palate function**	**PI that did not progress to DDSP**	**PI that progressed to DDSP**	**P value**
Concave depressions during inspiration				<0.001
None	0	29	27	
Small	0	7	4*	
Large	7	0	0	
Concave depressions during expiration				0.005
None	0	1	4	
Small	0	13	17 }**	
Large	7	22	10 }**	
Sling appearance				0.019
No	4	30	30	
Yes	3	6	1	
Flaccid				0.284
No	7	25	23	
Yes	0	11	8	
Billowing either side of epiglottis				0.340
No	7	26	24	
Yes	0	10	7	
Billowing in front of epiglottis				0.020
No	7	22	14	
Yes	0	14	17	

*of which 3 horses which were graded with depressions in the last ten seconds lost the depression in the two breaths immediately prior to DDSP
**7 horses which were graded with depressions in the last ten seconds lost the depressions in the two breaths immediately prior to DDSP.

There were significant differences between the size of the concave depression and presence of DDSP. Horses without DDSP had a mean maximum size of 60% and horses with DDSP a mean maximum size of 47% ($p=0.003$). When a midway percent of 54% was used to determine small or large depressions, 87% of the time this was the same value as had been assigned with the subjective grading (kappa 0.751, $p<0.001$).

There was a significant association between billowing of the soft palate and loss of inspiratory depressions ($p<0.001$).

Further analysis was performed on the 67 horses with palatal dysfunction to identify whether any characteristics were associated with progression from PI to DDSP. The results showed that both epiglottic conformation ($p=0.039$) and stability of the soft palate ($p=0.021$) were significantly associated with development of DDSP. Sixty three percent of horses with PI with rima glottidis obstruction progressed to DDSP compared with 34% of horses with PI with no rima glottidis obstruction. There was variation between horses as to how long the PI was present before progression to DDSP occurred. No horse with a convex epiglottis progressed to DDSP, 22% of horses with flattened epiglottis progressed to DDSP and 57% of horses in which the tip of the epiglottis was positioned at or higher than the base of the epiglottis progressed to DDSP. There was no significant association between the severity of ADAF and progression to DDSP. The conformation of the soft palate was not associated with development of DDSP, with the exception of caudal soft palate depressions on expiration ($p=0.039$). Eighty percent of horses with no depressions during expiration progressed to DDSP, 57% of horses with small depressions progressed to DDSP, where as only 31% of horses with large depressions during expiration progressed to DDSP. All but one horse had no inspiratory depression immediately prior to DDSP.

10.4 Discussion

In the study by Lane *et al.* (2006a) it was suggested that palatal instability was a manifestation of the same condition as DDSP, because all horses with DDSP had pre-existing PI. Furthermore, 38% of the horses with a diagnosis of PI had a specific history of 'gurgling' suggesting that these horses might be experiencing DDSP during racing that had not been reproduced during the treadmill exercise test. Barakzai and Dixon (2011) also suggested that PI was a 'milder' form of DDSP. Similar findings were observed in the overground endoscopy chapters whereby strenuous exercise tests were often needed for DDSP to occur, however PI might be observed under less strenuous conditions.

The aim of this study was to attempt to characterise PI more objectively. In this study a different cohort of horses was used to those included in the study by Lane *et al.* (2006a), however the results again showed that all horses exhibited palatal instability prior to DDSP. However there was variation between horses as to how long the PI was present before this progressed to DDSP. The results show that epiglottic conformation and soft palate stability are both associated with the progression of PI to DDSP, suggesting that PI (as defined by Lane *et al.* 2006a) does represent a preliminary stage of DDSP. Strand *et al.* (2009) also described a statistically significant association between PI and DDSP in harness racehorses.

The findings of this study are supportive of Ahern's (1999a) hypothesis. All horses diagnosed with normal upper airway function and stable soft palates showed concave depressions in the caudal soft palate. This concave appearance to the soft palate was more prevalent during expiration than during inspiration, which suggests that the OPS is harder to maintain in the face of negative airway pressures during inspiration. The loss of inspiratory depressions was associated with a diagnosis of palatal instability and the subsequent loss of the depressions during expiration was associated with progression of PI to DDSP.

Early reports suggested that the epiglottis functions as a rigid support to hold the soft palate in a ventral position (Haynes 1981; Linford *et al.* 1983). However, associations between a flaccid epiglottis during resting endoscopy and DDSP during treadmill endoscopy were not well supported by subsequent treadmill studies (Kannegieter and Dore 1995; Parente and Martin 1995; Rehder *et al.* 1995; Parente *et al.* 2002; Lane *et al.* 2006b). Furthermore, Holcombe *et al.* (1997b) demonstrated that during experimentally induced epiglottic retroversion the soft palate remained in a normal position, which implied that a functional epiglottis was not required to maintain soft palate stability. However this study was performed in normal horses. Clinical cases of epiglottic retroversion also occur without DDSP (Barakzai 2007a). Although assessment of the epiglottis during resting endoscopy may be unreliable, this study suggests that the epiglottic conformation during exercise is indeed associated with palatal instability and DDSP. It was noted that during exercise the epiglottis tended to progress from convex to flattened to concave in horses with palatal dysfunction. Horses in which the tip of the epiglottis was positioned at the same level or higher than the base of the epiglottic were significantly more likely to displace the soft palate. It is unclear whether the epiglottis is pushed dorsally by the soft palate or whether a change in epiglottic conformation subsequently affects the oropalatal seal leading to billowing of the soft palate and this warrants further investigation.

The flattened epiglottic shape described in this study appears similar to that observed with electrical stimulation of the hyoepiglotticus muscle (Holcombe *et al.* 2002). However, hyoepiglotticus contraction must occur during inspiration in normal horses at exercise to prevent epiglottic retroversion. It is unclear why in some horses the epiglottis retains a normal concave appearance, where as in others hyoepiglotticus contraction results in a flattened epiglottis shape. Lane *et al.* (2006a) suggested that as the soft palate lifts in cases of PI and contacts the ventral surface of the epiglottis, greater contraction of the hyoepiglotticus muscle then occurs leading to the flattened conformation; however this hypothesis has not been studied.

A possible association with ADAF and palatal dysfunction has previously been suggested (Parente *et al.* 1994; Parente 1997; Lane *et al.* 2006a; Strand *et al.* 2009). This study suggested that ADAF is associated with epiglottic conformation and the severity of the palatal instability. Similar findings were reported by Strand *et al.* (2009) in harness racehorses. The aryepiglottic folds simply comprise a doubled layer of mucous membrane with no muscular tissue (McCluskie *et al.* 2006). It is likely that elevation of the epiglottis reduces the tension on the aryepiglottic folds allowing them to collapse axially into the laryngeal lumen on inspiration.

It is also important to establish what degree of soft palate stability is 'normal' or 'optimal'. In this study 'normal' was defined when the soft palate showed no tendency to billowing or instability. However, it is acknowledged that a completely stable soft palate was relatively uncommon in this population of horses, as all were referred for abnormal noise and/or poor performance. It would be of value to investigate the stability of the soft palate in a large group of horses that are performing well. Furthermore it would be useful to understand the effect of palatal instability on ventilation and gas exchange.

It is unclear to what extent the severity of the billowing of the soft palate might vary with endoscope position. It is possible that the extent to which the rima glottidis is obscured appears more severe with a more rostrally positioned endoscope tip. It would be of value to position the endoscope in different locations in the same horses to study this further.

The main limitation of this study remains the subjective nature to grading or assessing PI. Numerous grading systems are used in veterinary research and clinical practice. Any system of grading that relies on the human eye is essentially subjective (Dyson 2011). This study showed satisfactory repeatability and reliability for the variables assessed and the results are similar to the findings for laryngeal function scores (Hackett *et al.* 1991; Perkins *et al.* 2009). However it should be noted that the two reviewers had spent an extensive period of time working together on clinical cases. A second limitation was the estimation of concave depressions in the soft palate on inspiration and expiration. Neither airway pressures nor footfall were measured, therefore accurate timing of inspiration or expiration could not be performed. Inspiration was judged by the caudal movement of the larynx as described by Tsukroff *et al.* (1998).

Although observation of PI remains subjective this study shows that certain characteristics of the soft palate and epiglottis are associated with progression to DDSP. In conclusion, it is likely that palatal dysfunction is a syndrome whereby palatal instability represents the preliminary stages of a disorder that may progress to DDSP.

Chapter 11 The effect of palatal dysfunction on measures of ventilation and gas exchange in thoroughbred racehorses during high-intensity exercise.

11.1 Introduction

The previous chapter suggested that palatal dysfunction was a syndrome whereby palatal instability represented the preliminary stages of a condition which can progress to dorsal displacement of the soft palate. Naturally occurring DDSP has been shown to affect ventilation, airflow, airway pressures and gas exchange during exercise (Rehder *et al.* 1995; Franklin *et al.* 2002a). Minute ventilation decreased by approximately 13%, primarily through a reduction in tidal volume, and maximal oxygen consumption decreased by 10% (Franklin *et al.* 2002a). Peak expiratory flows were significantly decreased, but there were no significant alterations in inspiratory flows (Franklin *et al.* 2002a). During periods of DDSP pharyngeal and tracheal inspiratory pressures became less negative, pharyngeal expiratory pressures became less positive and tracheal expiratory pressures became more positive (Rehder *et al.* 1995). Experimentally induced DDSP was also confirmed to increase expiratory impedance; however there were some differences in the observations compared with naturally occurring DDSP (Holcombe *et al.* 1998). The nasopharynx is a musculomembranous tube and other forms of nasopharyngeal collapse, such as dorsal and lateral pharyngeal wall collapse are thought to be detrimental to athletic performance. It has been shown that pharyngeal wall collapse affects ventilation parameters and arterial blood gases during exercise (Holcombe *et al.* 2001; Boyle *et al.* 2006; Durando *et al.* 2006). Interestingly, Durando *et al.* (2006) found that pharyngeal wall collapse was the disorder most commonly associated with blood gas abnormalities. Boyle *et al.* (2006) reported that palatal instability frequently occurred in conjunction with other forms of pharyngeal wall collapse. Therefore it would seem probable that narrowing of the nasopharynx solely due to a billowing soft palate would also have a detrimental effect on ventilatory parameters. Experimentally induced rostral PI was shown to have no significant effect on expiratory pharyngeal or tracheal pressures. However tracheal inspiratory pressures were significantly more negative and there was a trend for pharyngeal inspiratory pressures to be less negative, although this only approached statistical significance (Holcombe *et al.* 1997a). When horses with naturally occurring PI were compared to a group of normal horses and a group of DDSP horses (prior to displacement) no significant differences in ventilation or gas exchange were identified (Franklin 2002). Further research is needed to confirm whether any instability of the caudal aspect of the soft palate is itself performance limiting, or whether performance limitation is present only when DDSP has occurred.

The aim of this study was to assess to what degree different severities of naturally occurring palatal dysfunction affect ventilation and gas exchange during strenuous exercise.

11.2 Materials and Methods

A retrospective study was performed using data collected from thoroughbred racehorses with palatal dysfunction (Appendix IV). Only horses in which upper airway videoendoscopic recordings were made concurrently with measurements of ventilation were included. Horses with additional upper respiratory tract obstructions were excluded. However, in previous chapters and in other studies it was shown that there was an association between PI and axial deviation of the aryepiglottic folds (Parente *et al.* 1994; Tan *et al.* 2005; Lane *et al.* 2006a), therefore cases of mild ADAF were included (King *et al.* 2001). Horses in which the aryepiglottic folds collapsed beyond the vocal folds (i.e. moderate and severe ADAF) were excluded from this study (King *et al.* 2001). Horses in which DDSP only occurred briefly (<10 breaths) prior to correction were also excluded.

The purpose of the study was to assess palatal dysfunction in the caudal aspect of soft palate. In all cases the aim was to position the endoscope so that the tip was in line with the openings of the auditory tube diverticula (Lane *et al.* 2006a). However, horses in which the endoscope was positioned too far caudally (i.e. no soft palate was visible rostral to the tip of the epiglottis) and horses in which the endoscope was positioned too far rostrally (i.e. the rostral aspect of the soft palate was visible) were excluded.

Only horses undertaking a standardised incremental exercise test were included. Prior to exercise testing, horses were habituated to treadmill exercise during 3 training runs. A standardised incremental exercise test to fatigue was undertaken, consisting of 1 min at 6, 8 and 10 m/s on a

10% incline, followed by further increments of 1 m/s at 1 min intervals until the horse could no longer maintain pace with the treadmill.

The equipment used has previously been described (Franklin *et al.* 2002a). Briefly, during the exercise test, horses wore a close-fitting plastic facemask. Ultrasonic flow transducers[13] were mounted into the mask and were aligned over each nostril (figure 11.1).

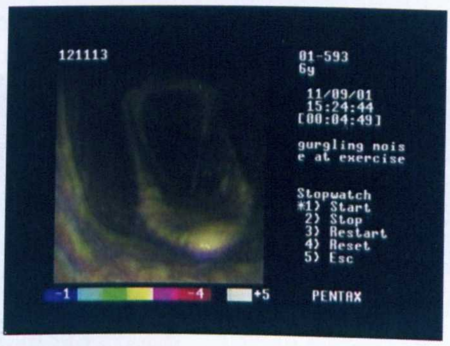
11.1 Image showing facemask with ultrasonic flow transducers placed over each nostril

The flow transducers were calibrated individually using a rotameter[14] before and after each exercise test. A flexible sampling capillary was positioned in the left flow tube. Continuous measurements of oxygen and carbon dioxide concentrations were made using a mass spectrometer[15]. Analysis of respiratory gas concentrations and airflow signals from both transducers were made on a breath-by-breath basis. The following respiratory and metabolic variables were calculated: minute ventilation ($\dot{V}_E$), tidal volume (V_T), breathing frequency (f), end-tidal carbon dioxide ($FetCO_2$) and oxygen ($FetO_2$) concentrations, oxygen consumption

($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$). Values for $\dot{V}_E$ and V_T were corrected to body temperature and pressure saturated and values for $\dot{V}O_2$ and $\dot{V}CO_2$ to standard temperature and pressure dry (STPD).

Simultaneous recordings of the videoendoscopic image and respiratory airflow were made during the exercise test (figure 11.2). In addition, a second video recording of the endoscopy image was made concurrently without the superimposed respiratory data (figure 11.3).

11.2 Simultaneous recording of videoendoscopy image and respiratory measurements

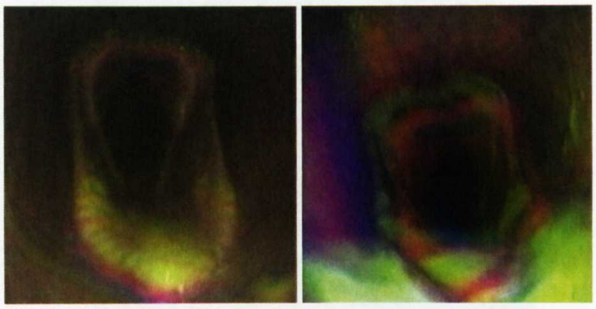


11.3 Same frame as figure 11.2 without superimposed respiratory measurements

The first recording was viewed to establish the time at which the respiratory data was to be retrieved. The second video was then watched to grade both the palatal dysfunction and ADAF, therefore at the time of grading the reviewer was blinded to the respiratory measurements. Analysis of the ventilatory parameters for individual horses was carried out by taking the mean of each variable during the 10 seconds prior to the cessation of the exercise test.

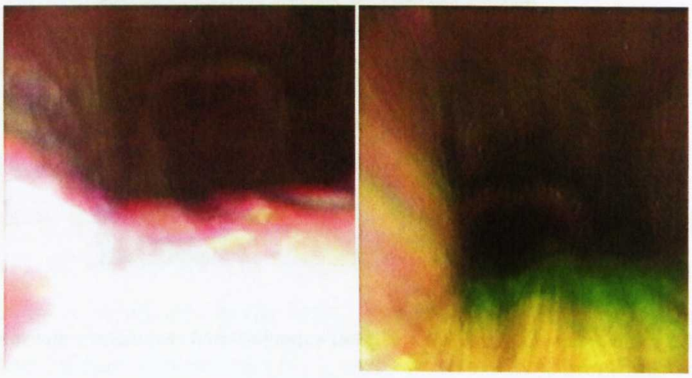
Three groups of soft palate function were formed:

1) Mild palatal instability – no rima glottidis obstruction



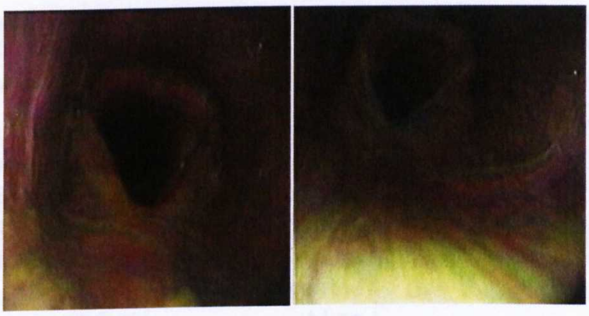
11.4 Images showing mild palatal instability without rima glottidis obstruction

2) Moderate to severe palatal instability – rima glottidis obscured by the billowing soft palate



11.5 Images showing moderate to severe palatal instability with the billowing soft palate obscuring the rima glottidis

3) Dorsal displacement of the soft palate- rima glottidis obstructed by the displaced soft palate



11.6 Images showing dorsal displacement of the soft palate

Statistical analysis was performed using PASW 18. The effect of soft palate dysfunction on variables measured during the exercise test was assessed using one way analysis of variance with Tukey's post hoc test. Chi- square test was used to compare the presence of ADAF between groups. A t-test was performed to assess the respiratory parameters for horses with no ADAF and those with ADAF in groups 1 and 2. Statistical significance was set at $P<0.05$.

11.3 Results

Forty horses were included in this study: 12 in group 1, 14 in group 2 and 14 in group 3. There were no significant differences between the groups for age, gender and type of racehorse (flat, National Hunt). There was no significant effect of run time, peak treadmill speed or bodyweight between groups.

Forty two percent of horses with mild palatal instability had ADAF, 57% of horses with moderate palatal instability had ADAF and 79% of DDSP horses had ADAF prior to the DDSP episode ($p=0.154$). For horses with PI, there were no significant differences in any measure of ventilation or gas exchange between those that had concurrent ADAF and those that did not.

The results show that minute ventilation and tidal volume decrease with increasing obstruction of the rima glottidis. End tidal carbon dioxide increases and end tidal oxygen decreases with increasing obstruction. Both oxygen consumption and carbon dioxide production decrease with increasing obstruction. For minute ventilation and tidal volume statistically significant differences were only seen with DDSP. However, both end tidal carbon dioxide and end tidal oxygen showed statistically significant differences between mild palatal instability and moderate to severe palatal instability.

Table 11.1 Ventilation, gas exchange and metabolic measurements in 40 horses with palatal dysfunction (mean ± sd). For each variable values with different superscripts are significantly different.

	Group 1 Mild palatal instability – no rima glottidis obstruction n=12	Group 2 Moderate and severe palatal instability – rima glottidis obscured by the billowing soft palate n=14	Group 3 Dorsal displacement of the soft palate- rima glottidis obstructed by the displaced soft palate n=14	P value
$\dot{V}_E$ (l/min)	2151 (342)[a]	2064 (285)[a]	1751 (223)[b]	0.002
V_T (l)	18.2 (3.1)[a]	17.7 (2.7)[a]	15.0 (2.4)[b]	0.011
$FetCO_2$ (%)	8.27 (0.75)[a]	9.02 (0.67)[b]	9.26 (0.35)[b]	0.001
$FetO_2$ (%)	13.45 (0.36)[a]	12.89 (0.55)[b]	12.41 (0.56)[c]	<0.001
f (breaths/min)	119.5 (7.2)	117.8 (5.4)	118.4 (8.6)	0.838
T_I (s)	0.254 (0.015)	0.257 (0.018)	0.250 (0.028)	0.726
T_E (s)	0.256 (0.017)	0.261 (0.013)	0.266 (0.024)	0.379
$\dot{V}O_2$ (ml/kg/min)	195.2 (11.1)	186.3 (11.8)	177.9 (26.1)	0.063
$\dot{V}CO_2$ (ml/kg/min)	213.2 (20.7)[a]	211.6 (20.4)	189.7 (28.9)[b]	0.025

11.4 Discussion

The aim of this study was to assess the effect of palatal dysfunction on measures of ventilation and gas exchange. It has previously been suggested that definitive assessment of the presence of an URT obstruction in an individual horse should only be made by quantitative determination of the effect of the obstruction on respiratory parameters (Kastner *et al.* 1998). However, in the clinical situation most horses undergo a diagnosis of URT obstruction based on subjective endoscopic observations alone without measurement of respiratory parameters. Therefore it would be of clinical value to determine the effect of several URT obstructions on measures of ventilation and gas exchange so that the relative importance of these conditions can be properly understood.

Ideally the effect of an URT obstruction on respiratory parameters would be determined by measurement of these parameters in the same horse with and without the obstruction. This approach has been used to show the effect of recurrent laryngeal neuropathy (RLN) on respiratory parameters. Ehrlich *et al.* (1995) showed a 15% reduction in peak $\dot{V}O_2$ with experimentally induced RLN compared with normal. However when a clinical cohort is used the effect of an URT obstruction may become less obvious. In the study by Christley *et al.* (1997) there was no significant difference in $\dot{V}O_{2max}$ with different grades of laryngeal hemiplegia when a clinical cohort was used. There are likely to be several reasons for this. Firstly there is a wide variation in respiratory parameters between individual horses. Secondly, for most studies the clinical cohort would comprise horses referred to a centre for poor athletic performance. Therefore even if no URT obstruction is present it is quite possible that the horse has a low $\dot{V}O_{2max}$ for another reason such as poor exercise capacity, cardiac arrhythmia, lower respiratory tract disease, lameness and gastric ulceration. Therefore, the use of a clinical cohort may be less likely to reveal statistically significant results, as larger numbers of horses are required to overcome population variability.

As DDSP is an intermittent event, Franklin *et al.* (2002a) were able to report the effect of DDSP on respiratory parameters in 9 horses with naturally occurring DDSP. By comparing the breaths before and after DDSP it was shown that DDSP resulted in a significant decrease in $\dot{V}_E$, V_T, $FetO_2$, $\dot{V}O_2$ and $\dot{V}CO_2$ and a significant increase in $FetCO_2$. This is not straightforward for PI which generally appears to be a progressive condition. It is unlikely that there is a clear cut off point between mild PI and moderate PI. Furthermore it is unclear whether experimentally induced PI is similar to the naturally occurring disorder and it is uncertain whether different degrees of severity could be reproduced using an experimental model.

Despite the potential difficulties of using a clinical cohort to study the effect of palatal dysfunction, this study did show that there was a trend for $\dot{V}_E$, V_T, $FetO_2$, $\dot{V}O_2$ and $\dot{V}CO_2$ to decrease and $FetCO_2$ to increase with increasing rima glottidis obstruction. Most of the variables showed statistically significant differences between PI and DDSP. However for $FetO_2$ and $FetCO_2$ there were statistically significant differences between the two grades of PI.

$FetO_2$ and $FetCO_2$ are non-invasive measures of gas exchange which are commonly used as an indirect measure of blood gases in human cardiopulmonary exercise testing. A reduction in $FetO_2$ and an increase in $FetCO_2$ occurs as a consequence of a reduction in alveolar ventilation (Franklin *et al.* 2002a). These changes are thought to be associated with an exacerbation of the arterial hypoxaemia and hypercapnia that occurs during strenuous exercise in horses. However, end tidal oxygen measurements may not be an accurate method for predicting P_aO_2 during exercise because of the widening of the alveolar – arterial PO_2 difference ($(A - a)PO_2$) (Bayly *et al.* 1987; Bayly *et al.* 1995; Wagner *et al.* 1989). End tidal CO_2 has been shown to be a good index of P_aCO_2 in healthy human patients at rest (Jones *et al.* 1979; Benallal and Busso 2000). Furthermore, Anderson *et al.* (1989) reported that $FetCO_2$ closely followed P_aCO_2 during exercise in healthy horses. Impaired gas exchange is critical to the equine athlete as the consequence is a decrease in $\dot{V}O_2$. Reduced ventilation limits the ability to expel carbon dioxide which accumulates in the body leading to hypercapnia which can be identified by increasing end tidal carbon dioxide. The falling $\dot{V}CO_2$ observed is not likely to reflect the true carbon dioxide production by the horse since horses continue to exercise at the same intensity and hence is in fact likely to be increased due to an increased reliance on anaerobic energy metabolism. However, the decrease in $\dot{V}_E$ results in a reduced ability to eliminate CO_2 from the body and hence the true $\dot{V}CO_2$ is underestimated, whilst $PaCO_2$ and $FetCO_2$ continue to increase. This suggests that both PI and DDSP are likely to be associated with impaired ventilation which consequently might affect athletic performance.

Of further interest is the wide range in measures such as $\dot{V}_E$ and $\dot{V}O_2$ which suggests that a superior equine athlete with a URT obstruction might still perform better than an inferior athlete with less/ no URT obstruction. It would seem likely that a stable URT is needed for an individual horse to have the opportunity to perform to its true ability. However, there was insufficient data to compare horses with mild PI to a group of normal horses with stable soft palates. Therefore it remains unclear to what degree mild PI might effect these parameters.

In this study only horses with mild ADAF were included. It was decided not to exclude all horses with ADAF as several studies have shown an association between ADAF and palatal dysfunction (Parente *et al.* 1994; Tan *et al.* 2005; Lane *et al.* 2006a) and this would have resulted in further exclusions. However, in order to reduce the effect of ADAF on the measures of ventilation, all horses with moderate or severe ADAF were excluded from the study. This data suggests that mild

ADAF did not further compromise measures of ventilation and gas exchange beyond that caused by the palatal instability.

In conclusion, the results suggest that PI with rima glottidis obstruction has a negative effect on respiratory parameters, although this is not as great as that associated with DDSP.

Chapter 12 The use of race performance analysis to assess interventions for dorsal displacement of the soft palate in British Thoroughbred racehorses.

12.1 Introduction

The results of the systematic review indicated that the method by which interventions for dorsal displacement of the soft palate were assessed affect the apparent success rates. Outcome measures should be valid, consistent and accurate for the condition being investigated. Race performance analysis is easily performed and the systematic review showed that there was a predominance of studies using this outcome measure. Most commonly race earnings were examined for the three races before and after the intervention (Anderson *et al.* 1995; Parente *et al.* 2002; Barakzai *et al.* 2004; Barakzai and Dixon 2005; Smith and Embertson 2005; Woodie *et al.* 2005a; Reardon *et al.* 2008a and b; Barakzai *et al.* 2009a). However, there are potential problems with the use of race earnings as an outcome measure. The inference is that improved racing performance occurs because of improvements in upper respiratory tract function. However, racing performance is multifactorial and is determined by the horses' ability, training, health and nutritional status and also by the ability of the jockey, type of race, ground conditions, number and ability of other horses and race tactics. Furthermore the multifactorial nature of poor athletic performance (Morris and Seeherman 1991; Martin *et al.* 2000) and the high prevalence of complex forms of URT collapse (Lane *et al.* 2006a; Barakzai and Dixon 2011) will also influence subsequent racing performance if these have not been accounted for. The fact that up to 36% variation in success rates were observed when the race performance measure and number of races assessed is altered casts serious doubt on the validity of this outcome measure. However, it is likely that performance analysis will continue to be widely used because of the ease of performing these studies. Therefore, it is important to fully understand the validity of race performance analysis to assess the efficacy of interventions and to confirm the appropriateness of this outcome measure.

Race earnings have been used to evaluate the efficacy of interventions for DDSP and for other conditions (Anderson *et al.* 1995; Duncan 1997; Bonenclark *et al.* 1999; Parente *et al.* 2002; Barakzai *et al.* 2004; Barakzai and Dixon 2005; Dykgraaf *et al.* 2005; Smith and Embertson

2005; Boyle *et al.* 2006; Parente *et al.* 2008; Reardon *et al.* 2008a; Barakzai *et al.* 2009a). Earnings have been suggested to account for the standard of the horses' performance in a race and the calibre of the race (Barakzai and Dixon 2005). Placings and its associated performance index have also been used to assess the efficacy of interventions for DDSP and for other conditions (Hawkins *et al.* 1997; Tulleners *et al.* 1997; Woodie *et al.* 2005a; Boyle *et al.* 2006; Taylor *et al.* 2006; Reardon *et al.* 2008a). Performance index is calculated by assigning a point value for the place of finish: first = 3 points, second = 2 points and third = 1 point (Woodie *et al.* 2005a). Ratings have been used in DDSP studies and to assess racehorse ability in other conditions (Jose-Cuneilleras *et al.* 2006; Reardon *et al.* 2008 a and b; Young *et al.* 2008; O'Meara *et al.* 2010). Ratings are assigned indices of racing performance which are utilized by the British racing authority for handicapping of horses and to aid the general public in assessing horses for betting purposes. In the UK several different rating systems are available. Official ratings (OR) are compiled by a team working for the British Horseracing Authority (www.britishhorseracing.com) and are used to determine the weights horses will carry in handicap races. Racing Post Ratings (RPR) are merit ratings produced by a team at the Racing Post (www.racing post.com) and are based on collateral form i.e. if horse A beats horse B carrying the same weight then it will be awarded a higher rating. The ratings are expressed in pounds (lbs) so a horse rated 140 is regarded as 10lbs better than one rated 130. There is a sliding scale for converting lbs to distance where 3lbs= 1 length over 5 furlongs and 1lb= 1 length over 2 miles or longer. Topspeed ratings (TS) are also produced by the team at Racing Post and are based on race times so horses recording faster times will achieve higher ratings. The ratings are measured in pounds (lbs) like RPR and aim to remove the effect of different going and weather conditions on the race times. Timeform ratings (TF) (www.timeform.com) are produced by a different team and also represent the merit of the horse expressed in pounds (lbs). It is arrived at by examination of horses' comparative performance using a scale of weight for distance beaten which ranges from around 3lbs a length at 5 furlongs and 2lbs a length at 1 mile and a quarter to 1lb a length at 2 miles. In contrast to RPR, TS and TF the OR reflect the horses' rating going into the race not what they achieved in the race. Official ratings and Racing post ratings use different scales for flat and NH horses, whereas Timeform ratings use different scales for flat, hurdles and fences.

Race times have been used to assess DDSP in Standardbred racehorses and for other conditions (Llewellyn and Petrowitz 1997; Roneus *et al.* 1997; Isgren *et al.* 2010). Sectional times allow measurement of speed over short distances typically at the end of the race (Hogan *et al.* 2002).

Studies from the US have suggested that variables such as age, breed, sex, track surface, gait, prize money, size of field, weight carried and start position affect race earnings or race times (Martin *et al.* 1996; Cheetham *et al.* 2010). However, there are important differences between racing in America and Britain, and this may further affect analysis of race performance. In Britain there are two types of thoroughbred races: flat and National Hunt (jumps) and about half the races each year are handicap races. Handicap races are set up to attempt to give each horse an equal chance of winning. The highest rated horse in the race carries the greatest weight, and inferior horses carry less weight. For most owners, handicap races offer the best chance of a horse winning a race.

It has previously been shown that trainers may use a tongue tie in races post surgical intervention (Barakzai *et al.* 2009b) and anecdotally it has been suggested that other factors such as racing over shorter distances and avoiding heavy going, may also be beneficial for horses diagnosed with DDSP (S.H. Franklin and J.G. Lane, personal communication).

The aim of this chapter was to explore the baseline racing characteristics in a group of horses confirmed to have DDSP. Race performance measures were compared to establish which parameter is best suited to this population, to identify whether these parameters are well correlated and how apparent success rates differ with each parameter. Furthermore the effect of various racing variables such as prize money, class, size of field, going and distance on the likelihood of earning in a race was assessed. Finally the data was analysed to establish whether there is any evidence that trainers alter these variables after a surgical intervention for DDSP has been performed.

12.2 Materials and Methods

Thoroughbred racehorses referred for abnormal noise and/or poor performance in which a diagnosis of DDSP only during high-speed treadmill exercise were included. Horses were included if any surgical intervention for DDSP was known to have been performed. Horses undergoing concurrent interventions i.e. for complex URT collapse were excluded. Horses must have raced three times before and after the intervention for inclusion.

Race earnings (RE), placings (Plc)(=finishing position 1-3), performance index (Perf. I) and ratings for the last three races before and first three races after the intervention were recorded. The following ratings were obtained Official rating, RacingPost rating, Topspeed rating and Timeform rating. For the purposes of analysis non earners, unrated and unplaced horses were assigned 0. Racetimes and sectional times were also investigated (www.turftrax.com). In addition, the time from surgery, type of race, race distance, prize, class of race, size of field, going, weight carried and whether a tongue tie was used were recorded for the six races for each horse.

Statistical analysis

Data were entered into a spreadsheet (Excel) and statistical analysis was performed using PASW 18. Each race performance variable was tested for normality using Kolmogorov-Smirnov statistic. Spearman rank correlation was used to assess the association between different ratings and between ratings and earnings. Kruskal Wallis tests were performed to assess whether Perf. I. and ratings were associated and whether Perf. I. and earnings were associated. Univariable binary logistic regression analysis was used to identify associations between race variables and the likelihood that money was earned in a race. Chi-square tests were used to compare class, handicap and going in the races before with the races after the intervention. Statistical significance was set at $P<0.05$.

12.3 Results

Baseline data

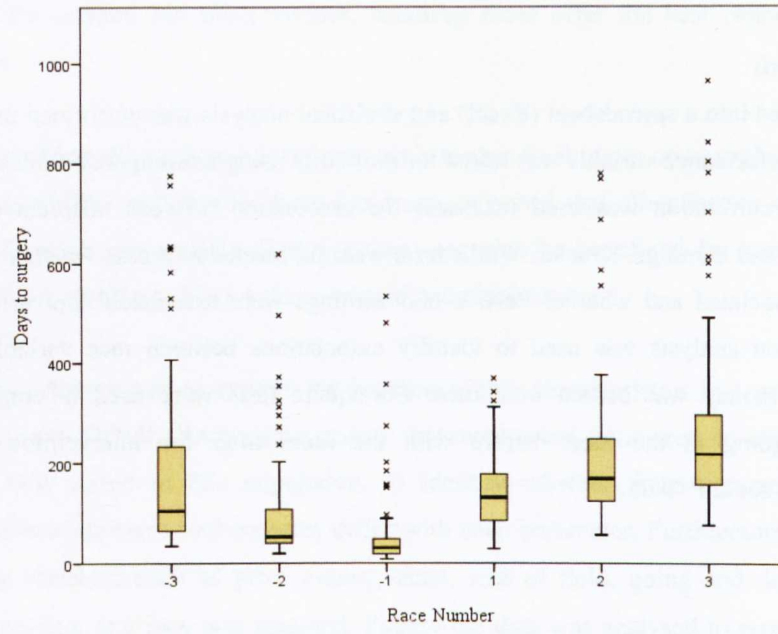
Of the 117 thoroughbred racehorses that met the inclusion criteria for diagnosis and intervention, 37 (32%) were subsequently excluded for not racing 3 times before and after the intervention. Therefore 80 horses (9 female, 71 male) were included. Ages ranged from 2-10 years, with a mean of 5 years. In 25 horses all six races were on the flat, in 38 horses all six races were NH and 17 horses were categorized as dual purpose i.e. the six races included flat and NH races. Flat races were run over 5 furlongs to 2 miles 1 f, carrying weights of 7 stone 4lbs to 11 stone 3lbs.

National Hunt races were run over 2 miles to 4 miles 1 furlong, carrying weights of 9 stone 7lbs to 12 stone.

Of the 480 races assessed, 62% of these were handicap races (77% of flat races and 53% of NH races). Sixty two races were run on an all-weather surface and 418 on turf.

Time between intervention and races

The days between each race and the surgery date are shown in figure 12.1. The median time to first race (+1) was 130 days (range 28-368 days). The median time from -3 race was 104 days and +3 race was 218 days. However, the third race before and after surgery varied up to 775 days before to 963 days after.



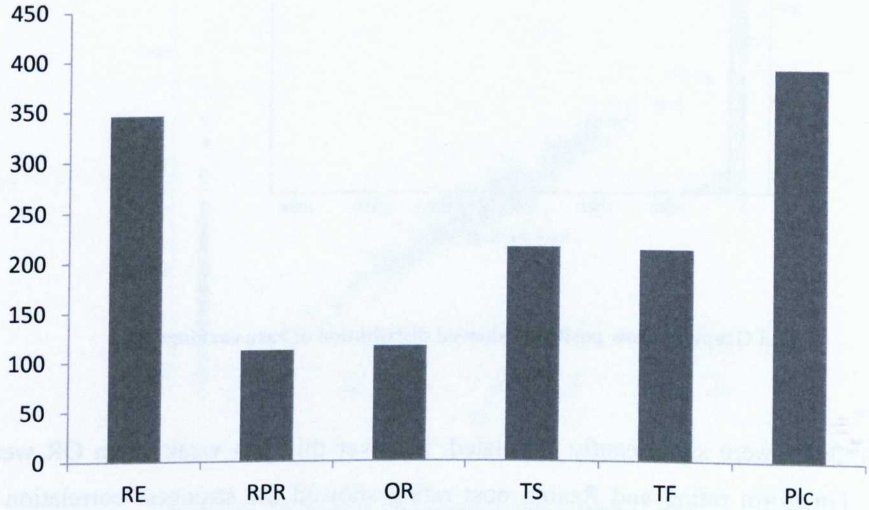
12.1 Boxplot showing median, interquartile range and outliers in the number of days from race to surgery

Race performance measures

In this population of horses race earnings, placings, performance index, official rating, racingpost rating, top speed rating and timeform rating were readily accessed. Race times were available for

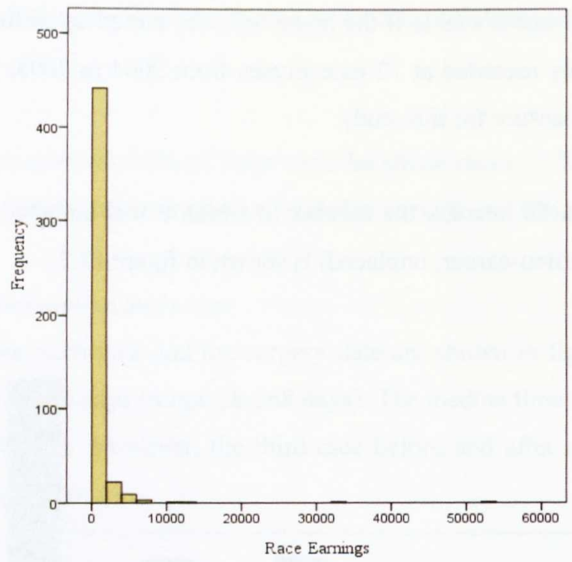
57% of races, however they were not available if the horse fell, was pulled up or for races run in Ireland. Sectional times were only recorded at 12 racecourses from 2004 to 2008, therefore this was not pursued as an outcome measure for this study.

For the total 480 races (6 races x 80 horses), the number in which 0 was assigned for earnings, ratings and placings (i.e. unrated, non-earner, unplaced) is shown in figure 12.2.



12.2 Graph to show the number of races in which 0 was assigned in the 480 races assessed. RE-race earnings, RPR – racingpost ratings, OR- official ratings, TS-topspeed ratings, TF- timeform ratings, Plc - placing

Placings contained the greatest number of 0 at 81% followed by race earnings in which 72% of the data had no earnings. As a result of the high numbers of 0 values, all measures showed a positively skewed distribution (figure 12.3).

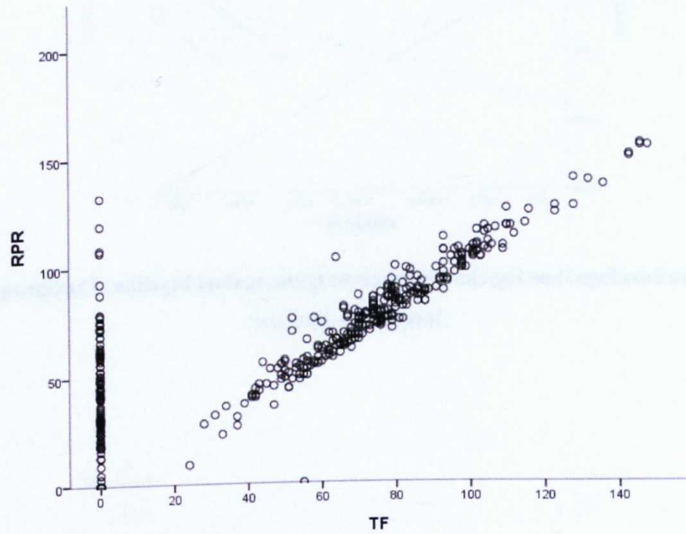


12.3 Graph to show positively skewed distribution of race earnings (£)

All ratings systems were significantly correlated, however this was weak when OR were used (table 12.1). Timeform rating and Racing post rating showed the strongest correlation (figure 12.4). No rating system was significantly correlated with race earnings.

Table 12.1 To show correlations between ratings systems and ratings and earnings

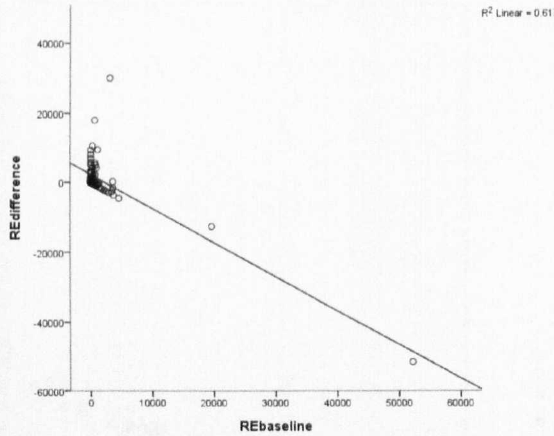
Variables assessed	Correlation coefficient	P value
RPR v OR	R=0.240	P<0.001
RPR v TS	R=0.687	P<0.001
RPR v TF	R=0.870	P<0.001
OR v TF	R=0.164	P<0.001
OR v TS	R=0.194	P<0.001
RE v RPR		P=0.119
RE v OR		P=0.353
RE v TS		P=0.379
RE v TF		P=0.200



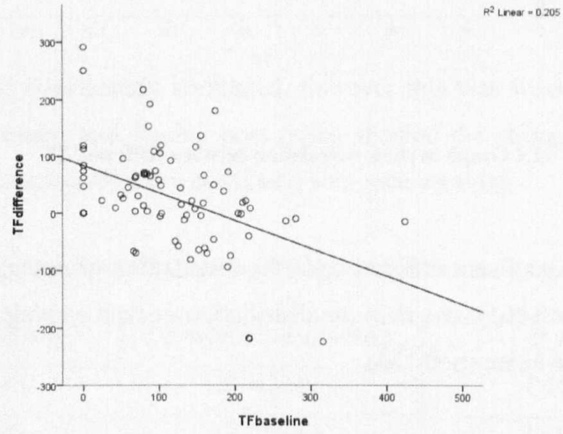
12.4 Graph to show correlation between RPR and TF

There were statistically significant differences in the distribution of ratings across the categories of performance index ($p<0.001$), however the distribution of race earnings was the same across categories of performance index ($p=0.134$).

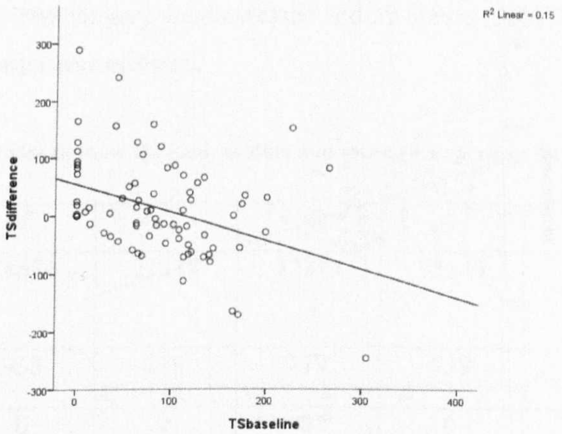
Scatterplots were produced to help identify regression to the mean. The change (follow-up (total value from races +1 to +3) minus baseline (total value from races -1 to -3)) was plotted against the baseline (total value from races -1 to -3). Some regression to the mean is apparent in the plots, as horses with higher baseline values have tended to decrease.



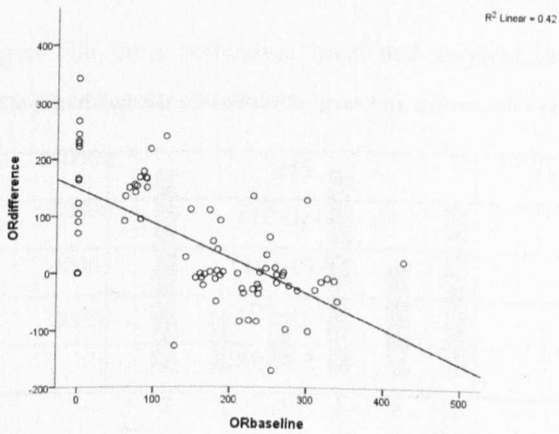
12.5 Scatter-plot of race earnings showing change minus baseline against baseline. The line represents the fitted regression line.



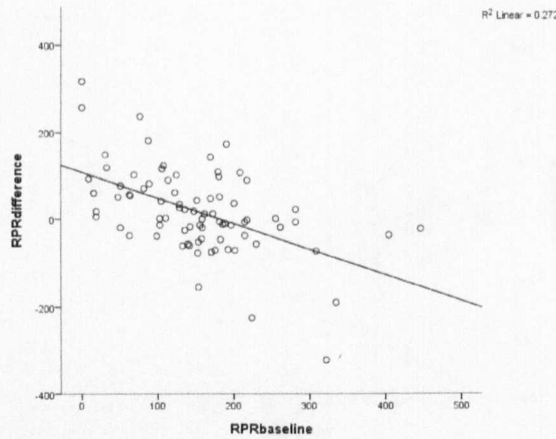
12.6 Scatter-plot of Timeform ratings showing change minus baseline against baseline. The line represents the fitted regression line.



12.7 Scatter-plot of Topspeed ratings showing change minus baseline against baseline. The line represents the fitted regression line.



12.8 Scatter-plot of Official ratings showing change minus baseline against baseline. The line represents the fitted regression line.



12.9 Scatter-plot of Racingpost ratings showing change minus baseline against baseline. The line represents the fitted regression line.

Different rating scales were assigned to horses in flat and NH races, and these were higher in NH (table 12.2).

Table 12.2 Shows the median and range of ratings for flat and National Hunt races.

Median Rating (range)	Flat	National Hunt
OR	64 (0-91)	90 (0-150)
RPR	58 (0-103)	85 (0-155)
TS	43 (0-92)	63 (0-138)
TF	64.5 (0-98)	84 (0-148)

Horses running in NH races were significantly more likely to be placed and to earn money than horses running in flat races. Included horses were placed in 13% of flat races compared with 22% of NH races ($p=0.011$). Included horses earned money in 20% of flat races compared with 33% of NH races ($p=0.002$).

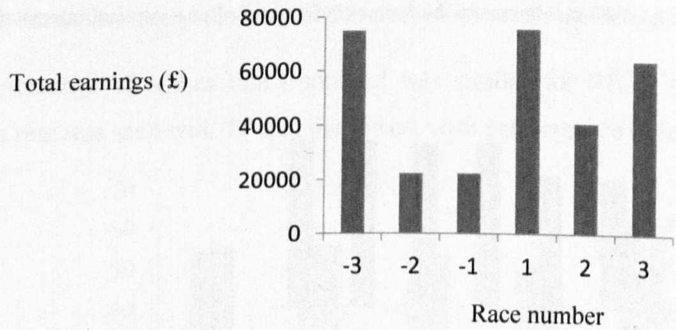
Apparent success of intervention

Forty five percent of horses earned money in the races before the intervention and 62% earned money in the races after the intervention. Forty four (55%) horses had improved earnings in the 3 races after surgery compared with the 3 races before. Forty horses (50%) had improved earnings when 2 races before and after surgery were assessed and 29 horses (36%) had improved earnings when 1 race before and after was assessed.

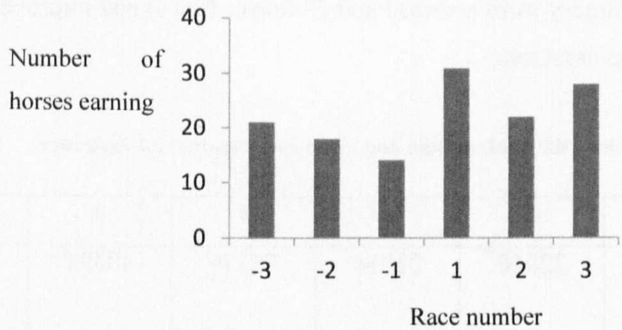
Table 12.3 Table to show the total, median and mean race earnings for each race

Race	-3	-2	-1	1	2	3
Total earnings (£)	74676	22348	22314	75149	40594	63629
Mean earning (£)	933	279	279	939	507	795
Median earning (£)	0	0	0	0	0	0
Number of horses that earn (n=80)	21	18	14	31	22	28

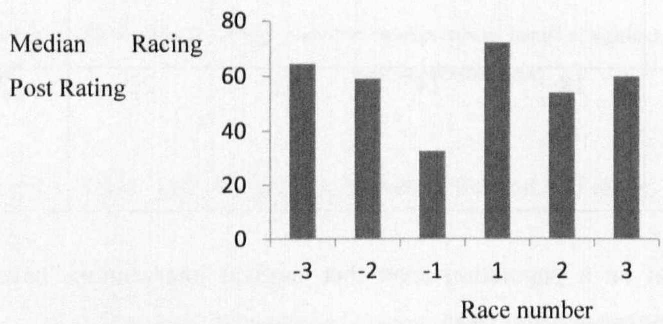
The graphs below suggest that on a population level that surgical interventions have some efficacy in improving race performance parameters.



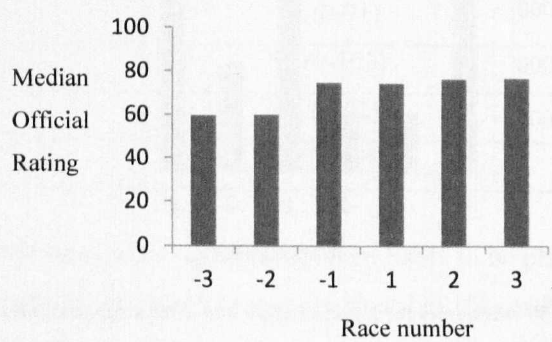
12.10 Total earnings for 80 racehorses for 3 races before and after a surgical intervention



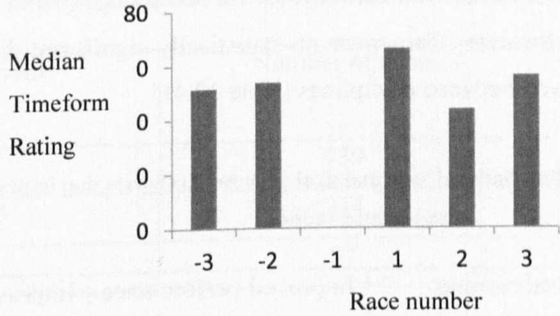
12.11 The number of horses earning in the 3 races before and after a surgical intervention



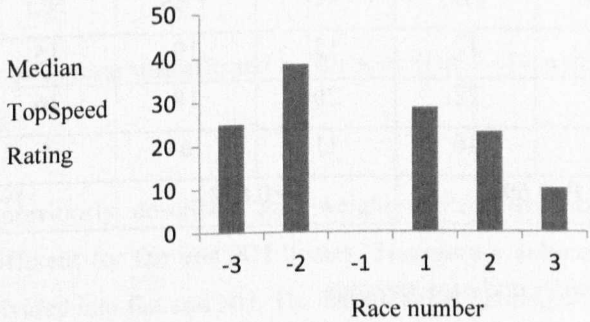
12.12 The median Racingpost rating for 80 racehorses in the 3 races before and after a surgical intervention



12.13 The median Official rating for 80 racehorses in the 3 races before and after a surgical intervention

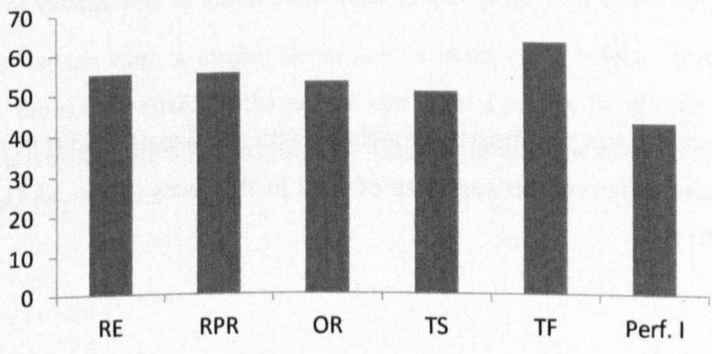


12.14 The median Timeform rating for 80 racehorses in the 3 races before and after a surgical intervention



12.15 The median Topspeed rating for 80 racehorses in the 3 races before and after a surgical intervention

The percentage of horses that improved was similar for RE, RPR, OR and TS. The greatest success rate was seen with TF and the lowest with performance index.



12.16 Graph to show the percentage of horses that improved following the intervention for different race performance measures

A greater proportion of NH horses improved earnings (58%) and ratings (58%) than flat horses (48% and 40% respectively). However, there were no statistically significant differences in the proportion of horses that improved between disciplines (table 12.4).

Table 12.4 Shows the number of flat, National hunt and dual purpose racehorses that improved following a surgical intervention

	Improved earning 3 v 3 races		Improved performance index 3 v 3 races		Improved Racingpost Rating 3 v 3 races	
	NO	YES	NO	YES	NO	YES
Flat	13	12	15	10	15	10
NH	16	22	20	18	16	22
Dual purpose	7	10	11	6	5	12
	P=0.696		P=0.672		P=0.131	

Associations between race variables and race earnings

An initial analysis was performed on the data for the total 480 races to identify any associations with the likelihood of earning money.

The likelihood of earning money in a race was affected by age ($p=0.008$), and discipline (flat/ NH) ($p=0.003$). As described previously horses were more likely to earn money in NH races than in flat races.

The likelihood of earning was significantly associated with the size of field (OR 0.91 $p<0.001$). There were significant difference between size of field in flat races (mean 13.4) and NH races (mean 11.7) ($p<0.001$).

Table 12.5 Shows the percentage of races in which horses earned money in relation to the size of field

Size of field	Number of races	Percentage of races in which horses earned
<10	139	42%
10-15	244	23%
>15	97	19%

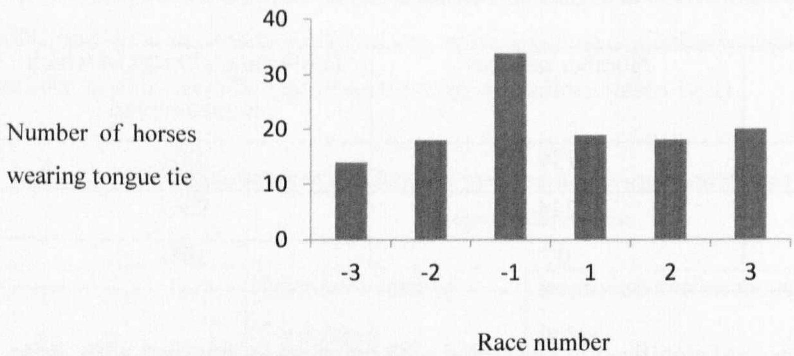
The likelihood of earning was not significantly associated with handicap racing ($p=0.459$), prize money on offer ($p=0.700$), class ($p=0.116$) or going ($p=0.503$).

The likelihood of earning was affected by distance (OR 1.054 $p=0.003$) and weight carried (OR 1.025 $p=0.001$).

However, as previously described age, weight carried, distance and size of field are all significantly different for flat and NH horses. Therefore a subsequent analysis was performed with the data divided into flat and NH. The likelihood of earning was not affected by age, gender, handicap, prize money on offer, going, distance, weight or class for either discipline. However size of field was significantly associated with likelihood of earning for NH horses (OR 0.895, $p=0.001$) but not for flat horses.

Tongue tie use

Forty two (53%) horses wore a tongue-tie in one or more races before surgery and 26 (33%) horses in one or more race after. Of the horses that wore a tongue tie on one or more occasion 70% were NH horses and 30% flat racehorses. Tongue tie use was greatest in the race prior to surgery (figure 12.17).



12.17 Shows the number of horses wearing a tongue tie in the 3 races before and after a surgical intervention

When horses wore a tongue tie in all 3 races post surgical intervention 70% had improved race earnings in the 3 races after compared with before. For horses that did not wear a tongue tie in all 3 races after 52% showed improved race earnings, however this was not a statistically significant difference (p=0.26).

Change in race variables following an intervention

Seventeen horses were raced in both NH and flat races during the 6 race study period. Seven horses raced in both disciplines in the 3 races before the intervention, 13 raced in both disciplines in the 3 races after the intervention and 3 horses raced in both disciplines before and after the intervention. The 17 dual purpose horses were removed from this section of the analysis. Therefore data from 63 horses was used and the variables for 189 (63 x 3) races before and 189 races after the intervention was compared.

Class: There was a trend towards decreasing class of race after surgery than before, however this only approached statistical significance (p=0.053).

Table 12.6 Shows the percentage of races of different classes before compared with after the intervention

Class of race	Races before intervention (-1 to -3)	Races after intervention (+1 to +3)
1-3	33%	26%
4	49%	44%
5-7	18%	30%

Prize money: there was no apparent change in prize money. The median win prize before and after was £3k.

Handicapping: 52% of races before the intervention were handicap races, where as 76% of races after the intervention were handicap races ($p<0.001$).

Weight: there was no apparent change in weight. The median weight before was 145 lbs and the median weight after 141lbs.

Going: For the 326 races run on grass, there appeared to be no significant change in the distribution of races on varying going ($p=0.188$).

Table 12.7 Shows the percentage of races on different going before and after a surgical intervention

Going	Races before intervention (-1 to -3)	Races after intervention (+1 to +3)
Firm	1.8%	3.8%
Good to firm	13.6%	22.9%
Good	40.8%	31.8%
Good to soft	20.1%	19.1%
Soft	16.0%	16.6%
Heavy	7.7%	5.7%

Distance: there was no apparent change in race distance. The median distance before and after was 16 furlongs.

Size of field: there was no apparent change in size of field. The median size of field before and after is 12 horses.

12.4 Discussion

Exclusions

Ideally design of intervention studies should ensure that a high proportion of the horses undergoing the intervention are subsequently analysed. One of the biggest concerns with the use of race earnings is the high proportion of horses that are excluded from analyses. For example, Woodie *et al.* (2005a) lost 47% and Reardon *et al.* (2008a) lost 56% of horses undergoing the intervention because they had not raced enough times. In this study restricting inclusion to 3 races before and after the intervention, as is most commonly done, resulted in 32% of horses not available for analysis.

There were significant differences in age, weight carried, distance and size of field between flat and NH. In the UK there are different rating systems for flat and NH horses. In this study population NH horses were more likely to earn money than flat horses. Therefore it is likely to be necessary to account for horses changing discipline within the analysis period. If dual purpose horses are also excluded (Reardon *et al.* 2008a), this would result in a further 21% of horses being lost from the analysis.

By designing a study that excluded horses that had not raced 3 times before and after the intervention and that changed discipline (flat/ NH) during this time, the analyses would be performed on only 46% of horses undergoing the intervention. This suggests that from the start the study design would be inappropriate and would be a weak intervention study.

Time frame

Several studies have reported the number of days from the intervention to the first post operative start (Anderson *et al.* 1995; Bonenclark *et al.* 1995; Duncan 1997; Ordidge 2001; Parente *et al.* 2002; Barakzai *et al.* 2004; Smith and Embertson 2005; Woodie *et al.* 2005a; Reardon *et al.* 2008a; Barakzai *et al.* 2009a). For UK studies, both Barakzai *et al.* (2004) and Reardon *et al.* (2008a) reported a large range in the time to first post operative race 38-812 days and 20-906 days respectively. The range in this study was 28-368 days. It is unclear to what degree the seasonality of UK racing might contribute to these time periods.

The median time to first surgery for other UK DDSP intervention studies was 73, 86, 137 and 168 days (Ordidge 2001; Barakzai *et al.* 2004; Reardon *et al.* 2008a; Barakzai *et al.* 2009a). The median time to first surgery in this study was 130 days, suggesting this data set is similar to that of other UK studies. However the time frame of the -3 and +3 races has not previously been reported. It is likely that assessing the efficacy of an intervention based upon a performance 900 days later might be inaccurate. The longer the time span the greater the potential for other factors such as other disease or other interventions to occur. To the authors knowledge no study set a time limit for races to occur for inclusion. This is a possible method to reduce the likelihood of other factors contributing to the race performance but will invariably cause further losses in the number of horses that are included.

Handicapping

Handicap races are designed so that better horses carry more weight than inferior horses, and therefore give inferior horses more chance of earning than in non-handicap races. Although it is suggested that handicapping gives owners of inferior horses better chances of earning, in this study no associations were identified which suggest that entering a horse in a handicap race increased the likelihood of that horse earning. However, there was a predominance of handicap races in this population, particularly in the races after the intervention. The fact that there was a significant increase in the proportion of horses running in handicap races after the intervention needs consideration. With handicap racing trainers can run horses that are not fit, over the wrong distance, or on a course or distance that does not suit the horse to further reduce the handicap. Therefore it is unclear when doing these analyses whether the horse is being entered in races so that the horse's handicap is further reduced, prior to entering it in a more suitable race with the aim of winning.

Race performance indices

Race earnings are the most commonly used race performance index. In this dataset for 72% of races there were no earnings. It is of questionable validity to use an outcome measure in which 72% of the total data is 0, as this affects the ability to detect change. As the data is highly skewed, the median should be used rather than the mean. Invariably the median for all races was 0. Some authors have log transformed earnings (log earnings +1) (Cheetham *et al.* 2008; Reardon *et al.* 2008a), however in this data set the high number of 0 still skew the transformed data.

In contrast to this data, the median value from the study by Cheetham *et al.* (2008) was an earning rather than 0. Therefore race earnings may be more appropriate in other countries than in the UK. It is unclear whether the differences occur because of different populations referred to different centres (Beard and Waxman 2007) or whether it is because of different distribution of race earnings. In UK race earnings are only awarded down to 4th or very occasionally 5th place. If in other countries prize money is awarded further down the field the use of race earnings may be more applicable. Although the differences were not statistically significant this study showed higher success rates with NH horses than with flat horses. This would suggest that in the UK where there is both flat and NH racing different success rates between centres might simply be due to different populations referred to each centre. It is unclear whether surgical interventions are more beneficial in NH horses or whether this observation is simply a reflection of the fact that these horses are more likely to earn than flat horses.

Placings and performance index had the highest number of 0 values, which suggests this is not a useful outcome measure in this population. Other UK studies have suggested that ratings may be more appropriate than race earnings or placings (Young *et al.* 2008). For example a horse placed fourth in an elite race is a better horse than one which wins a Class 6 race, however this would not be accounted for when using placings. Similarly a horses finishing just out of the earnings (5th) in a top race is also a better horse than one who comes fourth in a poor race earning as little as £250. Earnings and finishing position are dependent on an individuals performance relative to others, where as ratings reflect ability compared with the population as a whole (Young *et al.* 2008). For many ratings systems if the horse pulls up or performs poorly in a race a rating is not assigned. The nature of DDSP explains why there is still a high proportion of 0 even when using ratings as an outcome measure. Although ratings may be more appropriate than earnings and placings it is still not an ideal outcome measure.

Some race performance variables may be appropriate to use in studies where an estimate of the horses ability is required (Young *et al.* 2008), however for intervention studies it is important that the outcome measure changes quickly to reflect the success or not of the intervention. RPR and TF ratings showed a strong correlation and are likely to be better for use in intervention studies. OR are considered slow to change as is seen in this data and are not suitable for pre post intervention analysis.

Race times have been used in Standardbred racing (Llewellyn and Petrowitz 1997; Hogan *et al.* 2002). Racetimes were available for 57% of races but sectional times were very limited in availability. Racetimes were not recorded when the horse fell, pulled up or when it finished a long way behind the winner. In addition they were not available for races run in Ireland. Racetimes are probably not useful in UK thoroughbred racing, because of the variation in courses, going, distance and number of fences. Furthermore racetimes are difficult to compare between races because average speed decreases as race distance increase (Martin *et al.* 1996), therefore comparisons cannot be made if a horse ran 6 furlongs prior to an intervention and 8 furlongs after. Racetimes may be a more appropriate outcome measure in human track athletics as the tracks are better standardised. There is some evidence to suggest that tracks used in standardbred racing are standardised (Courouce *et al.* 1999), however this is not true for TB racing in the UK. It is also noteworthy that for most trainers the purpose of the race is not for the horse to perform as fast as possible, merely to perform faster than its rivals.

Success of intervention

The bar charts in this study present the data in a similar way to that used by Cheetham *et al.* (2008). The conclusions of that paper were that the procedure restores earnings to baseline level. This data could be interpreted the same way. For several of the outcome measures the data could be interpreted as the intervention was successful in restoring baseline characteristics (race -3). However when the percentage improvement using race earnings for 3 races before and after was assessed, the results were moderate (55%). Other UK surgical interventions have also shown poor to moderate results using race earnings for 3 v 3 races, 34% (Reardon *et al.* 2008a), 35% (Barakzai *et al.* 2009a) and 60% (Barakzai *et al.* 2004). By choosing how to present the data, i.e. the first format used by Cheetham *et al.* (2008) or the second format used by Barakzai *et al.* (2004, 2009a), the apparent efficacy of the intervention is affected. The way the authors choose to present the data can have a big effect on the conclusions of the apparent efficacy of the procedure.

Again there was some variation in the apparent success rate between outcome measures. This study and that of Reardon *et al.* (2008a) showed that performance index gave the lowest success rates. No study has accounted for the amount of improvement that would be clinically relevant. As previously described a horse only needs to earn £1 more after the intervention than before to be grouped in the success category.

When reporting the proportion of horses that improve many intervention studies typically compare 3 races before and after. In this study the decrease depends on the race parameter used but was most typically at the -2 or -1 race. The rationale of including data from the -3 race if horses were not poorly performing at this time has not been explored. It is likely that there will be variation between individual horses as well as between studies and perhaps it would be more appropriate to identify the drop in performance for that data set rather than use a standardised rule. The number of races examined before and after should be the same. Christley (2009) has described that with positively skewed data comparing one race before with three races after is mathematically incorrect and is likely to falsely imply success of an intervention.

Regression to the mean is a statistical phenomenon that occurs when repeated measures are made on the same subject (Barnett *et al.* 2005). For example horses with earnings at the extreme will tend to regress to the population mean of the group. All the variables assessed showed evidence of regression to the mean. In future intervention studies when comparing two treatment groups, analysis of covariance is one statistical method that can be used in the data analysis to deal with regression to the mean (Barnett *et al.* 2005).

Factors affecting race earnings

In a recent study from North America it was shown that age, breed, sex, track surface and gait affect race earnings and should be controlled for in the study design and analysis of race performance following an intervention (Cheetham *et al.* 2010). Martin *et al.* (1996) had previously shown that race times were increased with track surface, prize money on offer and age of horse and decreased with size of field, weight carried and start position. In both of these studies a large sample of the general population of racehorses were assessed, where as in this study a population known to be affected with DDSP was assessed. The principle factors that affect likelihood of earning (age, weight carried and distance) were associated with the different disciplines of flat and NH racing. In addition, the size of field was also particularly important in the likelihood of earning and this may need to be accounted for in intervention studies. With an ever increasing number of confounding variables having been identified, it is likely that this sort of statistical analysis is beyond the knowledge of many veterinary surgeons performing clinical practice research and the advice of a statistician should be sort.

It would be of value to confirm that the differences in earnings and placings between flat and NH was true for the general population and not just for the referral population to this hospital. The geographical location of the University of Bristol might mean that better quality NH horses are referred to the hospital than flat horses.

Change in variables following an intervention

In this study 53% of horses wore a tongue tie in one of the 3 races before compared with only 33% of horses after. Whereas, Barakzai *et al.* (2009b) found a similar proportion of horses using a tongue tie pre and post surgery of 39 and 41% respectively. In this study tongue tie use was greatest in the -1 race suggesting that trainers considered the tongue tie to be of limited efficacy. Similar to the findings of Barakzai *et al.* (2009b) continued tongue tie use post operatively may have some benefits, although the differences in results were not statistically significant. It is unclear whether tongue tie use in these cases is truly beneficial, or whether if a horse happens to perform well whilst wearing the tongue tie in the first post operative race the trainer might be reluctant to remove it for further races.

The most apparent changes before and after the intervention was a decrease in class of race and an increase in the proportion of handicap races. However, neither of these appeared to affect race earnings in this population. This analysis is attempting to identify changes which occur on a population level. It is possible that changes made to certain individuals might be highly influential in subsequent success rates, however if only small numbers of trainers are performing these they would not be detected in this study. Furthermore with the high proportion of handicap races in the UK it is unclear which horses are entered in races that they are hoped to be successful in and which horses are entered in races knowing they will not be successful.

This study has been unable to provide evidence to support anecdotally recommended alterations such as avoiding heavy going and running over shorter distances. It is probable that altering race distance/ going may work in some individuals but not others. Horses running over shorter distances and firmer surfaces will have to go faster in order to win. At present it is unclear whether inspiratory pressures or muscular fatigue is the more influential factor. Racing at faster speeds will be associated with greater negative inspiratory pressures, however racing longer distances and on heavier going is likely to have more affect on muscle fatigue.

Conclusions

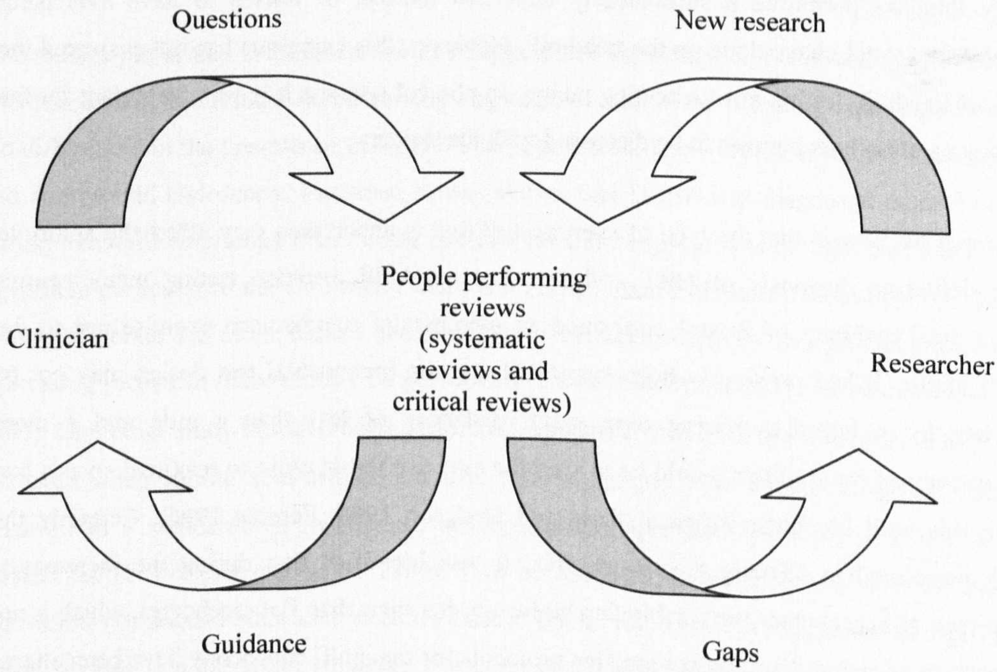
A suitable race performance outcome measure to assess interventions for palatal dysfunction needs to provide information that is well correlated with URT function and which also changes quickly from race to race. The race performance indices assessed in this study had a high proportion of 0 which suggest these are not ideal outcome measures. The high numbers of 0 mean that changes in performance may not be reliably detected. Of the outcome measures assessed ratings may be more appropriate for UK data, particularly RPR. Data suggest that several confounding factors exist when using race performance analysis which should to be accounted for in future studies.

In some medical conditions subjective and objective outcome measures are used together and this could be explored for DDSP. This would allow trainers to discuss in which races a particular horse was expected to do well in and confirm that no other interventions or that no other disease has occurred within that time frame.

Chapter 13 Discussion

Evidence based medicine involves a process of formulating questions, finding the evidence to answer the question, evaluating the evidence, implementing it in clinical practice and evaluating one's performance (Sackett *et al.* 2000).

To implement EBM in clinical practice we use the knowledge gained from research on populations to inform clinical decisions about individuals (Greenhalgh 2010). The aim of the thesis was to improve the quality of care of athletic horses afflicted with dynamic palatal dysfunction by promoting and utilising diagnostic and treatment practices that work and avoiding diagnostic and treatment practices that are ineffective or harmful. When good evidence is identified from undertaking reviews this should be fed to clinicians to improve clinical practice, where insufficient evidence is identified this should be fed back to researchers, so that gaps in our knowledge can be addressed.



13.1 Adapted from the healthcare knowledge figure of eight. In: Improving access to healthcare information in the developing world: a position paper for WHO (2004) F. Godlee, N. Packenham-Walsh, D. Ncaylyana, B. Cohen and A. Packer.

Unfortunately at present the quality of the evidence base for dynamic palatal dysfunction is weak which impacts on the ability of clinicians to practice EBM. With reference to the healthcare knowledge figure of eight (figure 13.1), it has been suggested that the quality (reliability, relevance and usability) of information available at each stage depends on the quality of information provided by the stage before. Therefore it was not possible in one thesis to transform a weak evidence base into a strong evidence base. This is likely to take years of further research, but it is hoped that a solid foundation has been started, upon which further work can be based.

In terms of implementing evidence into clinical practice, the results suggest that a diagnosis might be best obtained by combining information obtained from history, resting endoscopy and exercising endoscopy. The initial research undertaken in this thesis and the recent commercial availability of overground endoscopes has led to their widespread use in clinical practice. Certainly this has permitted a substantially increased number of horses to have exercising endoscopy than would have done on the treadmill. However, this technique has not answered the problem of treadmill testing not replicating racing. In clinical practice it is very important for the pros and cons of both techniques to be discussed with the trainer.

The research has shown that the type of exercise test that is undertaken may affect the ability to make a definitive diagnosis of URT collapse. For treadmill exercise testing many centres including the University of Bristol performed an incremental standardised exercise test to the point of fatigue. It had previously been suggested that the incremental test design may not be appropriate for a horse exercising over sprint distances of less than a mile and a more representative test for sprinters would be to start the exercise test at close to maximal speeds and maintain this until the horse fatigues (Rose and Hodgson 1994; Parente 1996). Certainly the research performed in Chapter 8 supports this. It was identified that during the incremental exercise tests NH racehorses were achieving higher speeds steps than flat racehorses, which is not representative of racing. Our clinical practice protocols for treadmill endoscopy have been altered such that the incremental tests are performed on NH horses and flat horses running over longer distances, and a single high speed test is now performed for flat horses racing over shorter distances.

For overground endoscopy, exercise tests are often performed at trainer's premises over routine training speeds and distances, therefore exercise tests are highly dependent on the facilities available at that training yard. This results in marked variation in the type (speed, distance, duration and number of intervals) of exercise performed and tests are very difficult to standardise between yards. As many U.K. trainers only undertake training on short inclined gallops, the speeds and distances experienced during overground endoscopy may not be the same as those experienced during racing. For flat horses, the distances performed during training may be more similar to race distances; however for National Hunt horses training distances are markedly shorter than the distances encountered during racing. Many horses are referred with a history of a problem (either abnormal noise or poor performance) occurring during racing and in these horses it may be difficult to recreate this problem on the training gallops. It is likely that many overground exercise tests performed under conditions similar to training, are not as strenuous and do not recreate the degree of fatigue the horse would experience during racing or that is more easily achieved during treadmill exercise testing.

The studies performed in Chapters 8 and 9 suggest that the design and application of appropriate exercise tests is the critical factor for the diagnosis of conditions affecting equine performance. No differences in the prevalence of dynamic laryngeal disorders were observed between treadmill and overground endoscopy. However, it was shown that DDSP was diagnosed more frequently during treadmill endoscopy than during overground endoscopy. It was thought that this might be a problem particular to the UK, where there is a predominance of short inclined gallops. In other countries, horses are often stabled and trained at racetracks, whereby overground exercise tests replicating races can more readily be performed (Davie and Evans 2000; Vermeulen and Evans 2006). One other study has also been performed comparing treadmill and overground endoscopy and even when similar standardised exercise tests to fatigue were attempted on the track and treadmill in 9 standardbred racehorses, different endoscopic findings were observed in some horses (van Erck-Westergren *et al.* 2009). Two horses experienced DDSP only on the treadmill and would not sustain strenuous exercise on the track (van Erck-Westergren *et al.* 2009). The reason for this is not certain. However it was proposed that behavioural factors were involved, whereby on the track the horses reduced their speed in order to prevent DDSP from occurring, where as during treadmill testing the horses were less able to reduce their speed (van Erck-Westergren, personal communication). The study in Chapter 9 was undertaken to attempt to identify what affect variation in overground exercise test parameters had on the diagnosis of URT obstructions. It was hoped that this information could be used to develop appropriate field exercise testing protocols. However, in this study there were no significant differences in exercise test parameters between horses with and without a diagnosis of URT obstruction. It is likely that URT collapse occurs when a combination of critical negative airway pressure is reached and when fatigue of the upper airway dilator muscles occurs. The finding that similar obstructions were observed irrespective of whether horses were referred for abnormal noise in training or abnormal noise in racing suggests between horse variations may be very important. For example, the inspiratory pressures and degree of fatigue required to induce an URT obstruction in one horse may be different than those required to induce the same abnormality in another horse. However when DDSP was specifically assessed, it was noted that for horses referred with abnormal noise during racing, DDSP was more likely to be observed if longer test distances (i.e. closer to race distances) were undertaken.

Therefore in clinical practice consideration of the presenting complaint is important when designing exercise tests. A different exercise test might be used in a horse referred for abnormal noise in training compared to one referred for abnormal noise in racing. Test distance appears to be a key factor. Therefore the best advice for horses that make abnormal noise only during a race or have poor race performance, is to replicate race conditions as closely as possible. In many circumstances this will require the use of a circular gallops (e.g. a racecourse or public training facility) if only short gallops are available at the trainer's premises. In addition, acknowledgement by veterinary surgeon, trainer and/or jockey as to whether the exercise test performed did replicate the presenting complaint is important. Horses in which the presenting complaint was not reproduced are less likely to have a diagnosis of URT obstruction. Therefore care should be taken interpreting a normal airway if the presenting complaint was not reproduced during the exercise test.

The research performed in Chapters 10 and 11 suggest that palatal instability represents a preliminary stage of dysfunction which can progress to DDSP. The results suggest that when palatal instability is observed in clinical practice that this may be detrimental to ventilation when rima glottidis obstruction occurs and that certain characteristics are suggestive that DDSP might occur under more strenuous conditions.

Unfortunately there is insufficient evidence upon which to make informed choices for treatment of palatal dysfunction. Decision making for choice of intervention is currently based on inadequate published data, personal experience or anecdote rather than on evidence based data. The evidence suggests that current treatments appear to be of limited efficacy. The systematic review has provided information on the key 'gaps in knowledge' which can be addressed by future research. There appears to be little value in undertaking more weak interventions studies. Research would be better directed towards understanding the pathophysiology before trying to develop new treatments. Furthermore, additional work should focus on determining the most appropriate outcome measures so that better quality intervention studies can be performed.

The research undertaken in this thesis concentrated on objective outcome measures. In the systematic review it was noted that very few studies had been undertaken using repeat exercising endoscopy. This is likely due to the costs of this type of study and the difficulties in recruiting cases. The development of overground endoscopy may enable more studies to be performed. However the issues regarding the exercise test need consideration. It is probable that in the UK this methodology would only enable conclusions to be made regarding the efficacy of the procedure under training conditions and not under racing conditions. The other difficulty with this outcome measure is that it remains uncertain what degree of palatal improvement should constitute a success. Although the research has not been able to fully answer this, the work in Chapters 10 and 11 suggest that interventions which prevent DDSP, even if PI remains should still result in some improvement. However when PI is still present, it is likely that ventilation might still be impaired compared to normal horses and that DDSP might be more likely to occur under more strenuous conditions compared to normal horses. Therefore interventions that result in a stable soft palate are likely to be more beneficial than procedures that prevent DDSP but in which PI is still observed.

With regards to racing performance the systematic review highlighted several concerns with this outcome measure. It was shown that return to racing is probably not a particularly useful outcome measure in populations of horses that could continue racing, for example with conditions such as DDSP. This outcome measure may be more appropriate for conditions such as orthopaedic injuries, where the horse is unable to race with that condition. Chapter 12 showed the skewed distribution of racing variables in the UK, and that in this population of horses much of the data is missing. It appears that several confounding factors have now been identified, which need to be accounted for in future studies. Further research is also needed on minimum clinically important differences (MCID) and effect size. Previous studies have used an increase of £1 for horses to be ranked in the success category which is not clinically relevant. In medicine the MCID represents the smallest improvement considered worthwhile by the patient (Copay *et al.* 2007). Rather than solely analysing whether differences between groups are statistically significant, research on effect size could also be used. Effect size is a way of quantifying the size of difference between two groups and is an important tool in reporting and interpreting effectiveness (Coe 2002).

Subjective outcome measures were not further researched in this thesis. Traditionally these have been perceived as less valid (Bent *et al.* 2009). However in medicine patient-reported measures have gained favour in recent years as they focus on issues important to patients (Bent *et al.* 2009). Similar to the results seen in the systematic review, in medicine there is also often poor correlation between subjective and objective outcome measures. However it has been suggested that although they provide different information, that information should be considered complementary and a combination of the two might provide the most comprehensive method of assessment (Bent *et al.* 2009). It would be useful to interview trainers and owners of horses with dynamic palatal dysfunction to identify their perceptions of success of an intervention. Following which a combined system could be developed utilising both subjective and objective outcome measures.

Following this research on outcome measures better intervention studies can be undertaken based upon definitively diagnosed cases, the results of which are assessed in a suitable manner. It would then be of considerable value to undertake a multicentre intervention study so that quicker progress can be made based upon larger numbers rather than small single centre studies. It is also important that adverse effects of treatments are better understood.

The fifth stage of evidence based medicine is self evaluation. For this thesis I attempted to review all publications related to the diagnosis, aetiopathogenesis and treatment of dynamic palatal dysfunction. In the future it may be more appropriate to ask smaller but more specific questions. This process has provided the opportunity to gain good knowledge in locating evidence, in understanding searching processes and having a good understanding of the best sources of current evidence. Understanding how to critically appraise the evidence has been a key step and where possible the knowledge gained has been integrated into clinical practice.

Manufacturers' addresses

1. RevMan Software, http://www.cc-ims.net/revman
2. Endnote, www.endnote.com
3. Veterinary Endoscopy Services, Southend-on-Sea, Essex. UK
4. EG-2990K, Pentax UK Ltd, Langley, Slough, UK
5. EPK-100p, Pentax UK Ltd, Langley, Slough, UK
6. PVR500r, DCS systems Ltd, St Wenn, Cornwall. UK
7. DV500, DCS systems Ltd, St Wenn, Cornwall. UK
8. Optomed, Les Ulis, France
9. VideoMed, Munich, Germany
10. Garmin Forerunner 305, Garmin, Olathe, Kansas, USA.
11. Polar S810i, Kempele, Finland.
12. Image J Software, rsbweb.nih.gov/ij/
13. BRDL Ltd., Birmingham, W.Midlands, UK.
14. KDG flowmeters, Burgess Hill, Kent, UK
15. Airspec QP9000, CASE Ltd, Gillingham, Kent, UK

References

Ahern, T. (1993a) Oral palatopharyngoplasty. *J. equine vet. Sci.* **13**, 185-188.

Ahern, T. (1993b) Oral Palatopharyngoplasty (part 2). *J. equine vet. Sci.* **13,** 670-672.

Ahern, T. (1999a) Pharyngeal dysfunction during exercise. *J. equine vet. Sci.* **19,** 226-231.

Ahern, T. (1999b) A breath away. (www.drtomahern.com)

Ahern, T.J. (2005a) Primary or secondary upper airways dysfunction? *J. equine vet. Sci.* **25**, 332-333.

Ahern, T. (2005b) Maximum tension palatoplasty. *J. equine vet. Sci.* **25**, 46-47.

Ainsworth, D.M., Eicker, S.W., Nalevanko, M.E., Ducharme, N.G., Hackett, R.P. and Snedden, K. (1996) The effect of exercise on diaphragmatic activation in horses. *Respir. Physiol.* **106**, 35-46.

Alkabes, K.C., Hawkins, J.F., Miller, M.A., Nauman, E., Widmer, W., Dunco, D., Kras, J., Couetil, L., Lescun, T. and Gautam, R. (2010) Evaluation of the effects of transendoscopic diode laser palatoplasty on clinical, histologic, magnetic resonance imaging, and biomechanical findings in horses. *Am. J. vet. res.* **71**, 575-582.

Allen, K.J., Lane, J.G., Woodford, N.S. and Franklin, S.H. (2007) Severe collapse of the rostral soft palate as a source of abnormal respiratory noise in six ponies and horses. *Equine vet. J.*, **39**, 562-566.

Amis, T.C., O'Neill, N., van der Touw, T. and Brancatisano, A. (1996a) Electromyographic activity of the hyoepiglotticus muscle in dogs. *Respir. Physiol.* **104**, 159-67.

Amis, T.C., O'Neill, N. and Brancatisano, A. (1996b) Influence of hyoepiglotticus muscle contraction on canine upper airway geometry. *Respir. Physiol.* **104,** 179-185.

Anderson, L.J. (1984) A study of some muscles of the equine larynx and soft palate. PhD Thesis Massey University, NZ.

Anderson, L.S., Butler, P.J., Roberts, C., Smale, K., Snow, D.H. and Woakes, A.J. (1989) Partial pressures of arterial and end tidal gases during graded exercise in thoroughbred racehorses. *J. Physiol.* **418**, 131.

Anderson, J.D., Tulleners, E.P., Johnston, J.K. and Reeves, M.J. (1995) Sternothyrohyoideus myectomy or staphylectomy for treatment of intermittent dorsal displacement of the soft palate in racehorses: 209 cases (1986-1991). *J. Am. vet. med. Ass.* **206**, 1909-1912.

Andrew, B.L. (1954) Proprioception at the joint of the epiglottis of the rat. *J. Physiol. (Lond)* **126,** 507–523.

Aragon, C.L., Hofmeister, E.H. and Budsberg, S.C. (2007) Systematic review of clinical trials of treatments for osteoarthritis in dogs. *J. Am. vet. med. Ass.* **230**, 514-521.

Arens, R. and Marcus, C.L. (2004) Pathophysiology of upper airway obstruction: a developmental perspective. *Sleep* **27**, 997-1019.

Art, T., Anderson, L., Woakes, A.J., Roberts, C., Butler, P.J., Snow, D.H., and Lekeux, P. (1990) Mechanics of breathing during strenuous exercise in Thoroughbred horses. *Respir. Physiol.* **82**, 279-294.

Art, T. and Lekeux, P. (1993) Training-induced modifications in cardiorespiratory and ventilatory measurements in thoroughbred horses. *Equine vet. J.* **25**, 532-536.

Art, T., Duvivier, D.H., van Erck, E., de Moffarts, B., Votion, D., Bedoret, D., Lejeune, J.P., Lekeux, P., and Serteyn, D. (2006) Validation of a portable equine metabolic measurement system. *Equine vet. J. Suppl.*, **36**, 557-561.

Attenburrow, D.P. (1978) Respiratory sounds recorded by radio-stethoscope from normal horses at exercise. *Equine vet. J.* **10**, 176-179.

Bangsbo, J., Iaia, F.M. and Krustrup, P. (2008) The Yo-Yo Intermittent Recovery Test: A Useful Tool for Evaluation of Physical Performance in Intermittent Sports. *Sports Med.* **38**, 37-51.

Barakzai, S.Z., Johnson, V.S., Baird, D.H., Bladon, B. and Lane, J.G. (2004) Assessment of the efficacy of composite surgery for the treatment of dorsal displacement of the soft palate in a group of 53 racing Thoroughbreds (1990-1996). *Equine vet. J.* **36**, 175-179.

Barakzai, S.Z. and Dixon, P.M. (2005) Conservative treatment for thoroughbred racehorses with intermittent dorsal displacement of the soft palate. *Vet. Rec.* **157**, 337-340.

Barakzai, S. (2007a) Treadmill endoscopy. In: *Equine respiratory medicine and surgery.* Eds: B.C., McGorum, P.M. Dixon, N.E. Robinson and J. Schumacher. Saunders. pp 235-248.

Barakzai, S. (2007b) Larynx. In: *Handbook of equine respiratory endoscopy.* Ed: S. Barakzai. Saunders. pp 67-88.

Barakzai, S.Z., Boden, L.A., Hillyer, M., Marlin, D. and Dixon, P. (2009a) Efficacy of thermal cautery for intermittent dorsal displacement of the soft palate as compared to conservatively treated horses: Results from 78 treadmill diagnosed horses. *Equine vet. J.* **41**, 65-69.

Barakzai, S.Z., Finnegan, C., Dixon, P.M., Hillyer, M.H. and Boden, L.A. (2009b) Use of tongue ties in thoroughbred racehorses in the United Kingdom, and its association with surgery for dorsal displacement of the soft palate. *Vet. Rec.* **165**, 278-281.

Barakzai, S.Z. and Hawkes, C.S. (2010) Dorsal displacement of the soft palate and palatal instability. *Equine vet. Educ.* **22**, 253-264.

Barakzai, S.Z. and Dixon, P.M. (2011) Correlation of resting and exercising endoscopic findings for horses with dynamic laryngeal collapse and palatal dysfunction. *Equine vet. J.* **43**, 18-23.

Barnett, A.G., van der Pols, J.C. and Dobson, A.J. (2005) Regression to the mean: what it is and how to deal with it. *Int. J. Epidemiol.* **34**, 215-220.

Barrey, E., Galloux, P., Valette, J.P., Auvinet, B. and Wolter, R. (1993a) Stride characteristics of overground versus treadmill locomotion in the saddle horse. *Acta Anat.* **146**, 90-94.

Barrey, E., Galloux, P., Valette, J.P., Auvinet, B. and Wolter, R. (1993b) Determination of the optimal treadmill slope for reproducing the same cardiac response in saddle horses as overground exercise conditions. *Vet. Rec.* **133**, 183-185.

Bayly, W.M., Grant, B.D. and Modransky, P.D. (1984) Arterial blood gas tensions during exercise in a horse with laryngeal hemiplegia before and after corrective surgery. *Res. vet. Sci.* **36**, 256-258.

Bayly, W.M., Schulz, D.A., Hodgson, D.R., Gollnick, P.D. (1987) Ventilatory response to exercise in horses with exercise-induced hypoxemia. In: *Equine Exercise Physiology*, 2nd Ed. Ed: J.R. Gillespie and N.E. Robinson, ICEEP Publications, Davis, CA. pp 172-182.

Bayly, W., Schott II, H., Slocombe, R. (1995) Ventilatory responses of horses to prolonged submaximal exercise. *Equine vet. J. Suppl.* **18**, 23-28.

Beard, W.L., Holcombe, S.J., and Hinchcliff, K.W. (2001) Effect of a tongue-tie on upper airway mechanics during exercise following sternothyrohyoid myectomy in clinically normal horses. *Am. J. vet. res.* **62**, 779-782.

Beard, W.L. and Waxman, S. (2007) Evidence based upper respiratory tract surgery. *Vet. Clin. N. Am.: Equine Pract.* **23**, 229-242.

Becker, A.C., Horner, N.T. and Holcombe, S.J. (1999) The effect of hyoid muscle traction on hyoid apparatus and epiglottic position and nasopharyngeal dimension. *Proceedings of the veterinary comparative respiratory society* (www.the-vcrs.org). (Downloaded 10/2008).

Benallal, H. and Busso, T., (2000) Analysis of end-tidal and arterial Pco_2 gradient using a breathing model. *Eur. J. Appl. Physiol.* **83**, 402-408.

Bent, N.P. Wright, C.C., Rushton, A.B. and Batt, M.E. (2009) Selecting outcome measures in sports medicine: a guide for practitioners using the example of anterior cruciate ligament rehabilitation. *Br. J. Sports Med.* **43**, 1006-1012.

Berger, G, Finkelstein, Y, Ophir, D. (1999) Histopathologic changes of the soft palate after laser-assisted uvulopalatoplasty. *Arch. Otolaryngol. Head Neck Surg.* **125**, 786-790.

Blythe, L.L., Cardinet, G.H., 3rd, Meagher, D.M., Brown, M.P. and Wheat, J.D. (1983) Palatal myositis in horses with dorsal displacement of the soft palate. *J. Am. vet. med. Ass.* **183**, 781-785.

Bonenclark, G., Bryant, J., Hernandez, J., Ferrell, E.P. and Colahan, P.C. (1999) Sternothyroideus tenectomy or sternothyroideus tenectomy with staphylectomy for the treatment of soft palate displacement. *Proc. Am. Ass. equine Practnrs.* **45**, 85-86.

Bossuyt, P.M., Reitsma, J.B., Bruns, D.E., Gatsonis, C.A., Glasziou, P.P., Irwig, L.M., Lijmer, J.G., Moher, D., Rennie, D. and de Vet, H.C. (2003) Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Standards for Reporting of Diagnostic Accuracy. *Br. Med. J.* **326,** 41-44.

Boyd, J.H., Petrof, B.J., Hamid, Q., Fraser, R. and Kimoff, R.J. (2004) Upper airway muscle inflammation and denervation changes in obstructive sleep apnea. *Am. J. Respir. Crit. Care Med.* **170,** 541-546.

Boyle, A.G., Martin, B.B., Jr., Davidson, E.J., Durando, M.M., and Birks, E.K. (2006). Dynamic pharyngeal collapse in racehorses. *Equine vet. J. Suppl.,* **36,** 546-550.

Bracher, A., Coleman, R., Schnall, R. and Oliven, A. (1997) Histochemical properties of upper airway muscles: comparison of dilator and nondilator muscles. *Eur. Respir. J.* **10,** 990-3.

Bradford, A., McGuire, M. and O'Halloran, K.D. (2005) Does episodic hypoxia affect upper airway dilator muscle function? Implications for the pathophysiology of obstructive sleep apnoea. *Respir. Physiol. Neurobiol.* **147,** 223-234.

Brancatisano, A., van der Touw, T., O'Neil, N. and Amis, T.C. (1996) Influence of upper airway pressure oscillations of soft palate electromyographic activity. *J. Appl. Physiol.* **81,** 1190-1196.

Brietzke, S.E. and Mair, E.A. (2004) Injection snoreplasty: investigation of alternative sclerotherapy agents. *Otolaryngol. Head Neck Surg.* **130,** 47-57.

Brown, D.C. (2008) Outcome measures in veterinary surgery: the good, the bad and the ugly. *Proceedings of the American College of Veterinary Surgeons Symposium.* (www.acvs.org). (Downloaded 01/2010).

Burn, J.F., Claydon, M., Morgan, J.E. and Franklin, S.H. (2006) A novel system for videoendoscopy of the upper respiratory tract. *Proceedings of the British Equine Veterinary Association.* **45,** pp 322.

Butler, P.J., Woakes, A.J., Smale, K., Roberts, C.A., Hillidge, C.J., Snow, D.H. and Marlin, D.J. (1993) Respiratory and cardiovascular adjustments during exercise of increasing intensity and during recovery in thoroughbred racehorses. *J. exp. Biol.* **179,** 159-180.

Carrera, M., Barbe, F., Sauleda, J., Tomas, M., Gomez, C. and Agusti, A.G. (1999) Patients with obstructive sleep apnea exhibit genioglossus dysfunction that is normalized after treatment with continuous positive airway pressure. *Am. J. Respir. Crit. Care Med.* **159,** 1960-1966.

Cehak, A., Deegan, E., Drommer, W., Lutkefels, E., and Ohnesorge, B. (2006) Transendoscopic injection of poly-L-lactic acid into the soft palate in horses: a new therapy for dorsal displacement of the soft palate? *J. equine vet. Sci.* ***26,*** 59-66.

Chalmers, T.C., Levin, H., Sacks, H.S., Reitman, D., Berrier, J. and Nagalingam, R. (1987) Meta-analysis of clinical trials as a scientific discipline I: Control of bias and comparison with large co-operative trials. *Stat. Med.* **6,** 315-328.

Chalmers, H.J., Cheetham, J., Yeager, A.E. and Ducharme, N.G. (2006) Ultrasonography of the equine larynx. *Vet. Radiol. Ultrasound.* **47**, 476-481.

Chalmers, H.J., Yeager, A.E., Ducharme, N. (2009) Ultrasonographic assessment of laryngohyoid position as a predictor of dorsal displacement of the soft palate in horses. *Vet. Radiol. Ultrasound.* **50,** 91-96.

Cheetham, J., Pigott, J.H., Thorson, L.M., Mohammed, H.O. and Ducharme, N.G. (2008) Racing performance following the laryngeal tie-forward procedure: A case-controlled study. *Equine vet. J.* **40,** 501-507.

Cheetham, J., Pigott, J.H., Hermanson, J.W., Campoy, L., Soderholm, L.V., Thorson, L.M. and Ducharme, N.G. (2009) Role of the hypoglossal nerve in equine nasopharyngeal stability. *J. Appl. Physiol.* **107,** 471-477.

Cheetham, J., Riordan, A.S., Mohammed, H.O., McIlwraith, C.W. and Fortier, L.A. (2010) Relationship between race earnings and horse age, sex, gait, track surface and number of race starts for Thoroughbred and Standardbred racehorses in North America. *Equine vet. J.* **42,** 346-350.

Cheng, S., Butler, J.E., Gandevia, S.C., and Bilston, L.E. (2008) Movement of the tongue during normal breathing in awake healthy humans. *J. Physiol.* **586,** 4283-4294.

Christley, R. (2009) Parameters derived from racing records to investigate the effect of surgical interventions. *Equine vet. J.* **41,** 831.

Christley, R., Hodgson, D.R., Evans, D.L. and Rose, R.J. (1997) Cardiorespiratory responses to exercise in horses with different grades of idiopathic laryngeal hemiplegia. *Equine vet. J.* **29,** 6-10.

Coe, R. (2002) It's the effects size, stupid. What effect size is and why it is important. *Proceedings of the Annual Conference of the British Educational Research Association.*(http://www.leeds.ac.uk/educol/documents/00002182.htm. Downloaded 08/2011).

Cook, W.R. (1962). Clinical observations on the equine soft palate. *Proceedings of the 1st British Equine Veterinary Association* 5-9.

Cook, W. R. (1965) The Diagnosis of Respiratory Unsoundness in the Horse. *Vet. Rec.* **77,** 516-527.

Cook, W. R. (1981) Some observations on form and function of the equine upper airway in health and disease. 1: The Pharynx. *Proc. Am. Ass. equine Practnrs* **27,** 355-389.

Cook, W. R. (2002) Bit induced asphyxia in the horse. *J. equine vet. Sci.* **22,** 7-14.

Copay, A.G., Subach, B.R., Glassman, S.D., Polly Jr, D.W. and Shuler T.C. (2007) Understanding the minimum clinically important difference: a review of concepts and methods. *Spine J.* **7,** 541-546.

Cornelisse, C.J., Holcombe, S.J., Derksen, F.J., Berney, C., and Jackson, C.A. (2001a). Effect of a tongue-tie on upper airway mechanics in horses during exercise. *Am. J. vet. Res.* **62,** 775-778.

Cornelisse, C.J., Rosenstein, D.S., Derksen, F.J., and Holcombe, S.J. (2001b). Computed tomographic study of the effect of a tongue-tie on hyoid apparatus position and nasopharyngeal dimensions in anesthetized horses. *Am. J. vet. Res.* **62,** 1865-1869.

Courey, M.S., Fomin, D., Smith, T., Huang, S., Sanders, D. and Reinisch, L. (1999) Histologic and physiologic effects of electrocautery, CO_2 laser and radiogrequency injury in the porcine soft palate. *Laryngoscope.* **109,** 1316-1319.

Courouce, A., Geffroy, O., Barrey, E., Auvinet, B. and Rose, R.J. (1999) Comparison of exercise tests in French trotters under training track, racetrack and treadmill conditions. *Equine vet. J. Suppl.* **30**, 528-532.

Courouce, A., Corde, R., Valette, J.P., Cassiat, G., Hodgson, D.R. and Rose, R.J. (2000) Comparison of some responses to exercise on the track and treadmill in French trotters: determination of the optimal treadmill incline. *Vet. J.* **159**, 57-63.

Courouce-Malblanc, A., Deniau, V., Rossignol, F., Corde, R., Leleu, C., Maillard, K., Pitel, P.H., Pronost, S. and Fortier, G. (2010) Physiological measurements and prevalence of lower airway diseases in Trotters with dorsal displacement of the soft palate. *Equine vet. J. Suppl.* **38**, 246-255.

Currell, K. and Jeukendrup, A.E. (2008) Validity, reliability and sensitivity of measures of sporting performance. *Sports Med.* **38**, 297-316.

Curtis, R.A., Kusano, K. and Evans, D.L. (2006) Observations on respiratory flow strategies during and after intense treadmill exercise to fatigue in thoroughbred racehorse. *Equine vet. J. Suppl.* **36,** 567-572.

Dart, A.J., Dowling, B.A., Hodgson, D.R. and Rose, R.J. (2001) Evaluation of high-speed treadmill videoendoscopy for diagnosis of upper respiratory tract dysfunction in horses. *Aust. Vet. J.* **79**, 109-112.

Dart, A.J. (2006) Vocal fold collapse after laryngeal tie-forward correction of dorsal displacement of the soft palate. *Vet. Surg.* **35**, 584-585.

Davidson, E.J., Martin, B.B., Boston, R.C. and Parente, E.J. (2011) Exercising upper respiratory videoendoscopic evaluation of 100 nonracing performance horses with abnormal respiratory noise and/or poor performance. *Equine vet. J.* **43,** 3-8.

Davie, A.J. and Evans, D.L. (2000) Blood lactate responses to submaximal field exercise tests in thoroughbred horses. *Vet. J.* **159,** 252-258.

den Herder, C., van Tinteren, H. and de Vries, N. (2005) Hyoidthyroidpexia: a surgical treatment for sleep apnea syndrome. *Laryngoscope.* **115**, 740-745.

Derksen, F.J., Robinson, N.E. and Holcombe, S.J. (1999) The upper airway as a conduit for air flow. In: Equine Surgery 2nd Ed. Eds: J.A. Auer and J.A. Stick. Saunders. Philadelphia. pp 307-313.

Derksen, F.J., Holcombe, S.J., Hartmann, W., Robinson, N.E., and Stick, J.A. (2001) Spectrum analysis of respiratory sounds in exercising horses with experimentally induced laryngeal hemiplegia or dorsal displacement of the soft palate. *Am. J. vet. Res.* **62**, 659-664.

Derksen, F.J. (2007) Evaluation of upper respiratory tract sounds. In: *Equine respiratory medicine and surgery.* Eds: B.C., McGorum, P.M. Dixon, N.E. Robinson and J. Schumacher. Saunders. pp 249-254.

Desmaizieres, L.M., Serraud, N., Plainfosse, B., Michel, A. and Tamzali Y. (2009) Dynamic respiratory endoscopy without treadmill in 68 performance Standardbred, Thoroughbred and saddle horses under natural training conditions. *Equine vet. J.* **41**, 347-353.

de Vries, N. and Verse, T. (2010) Hyoid suspension In: *Surgery for sleep disordered breathing*, 2nd Ed. Eds: K. Hormann and T. Verse. Springer. pp 143-153.

Dick, T.E. and Van Lunteren, E. (1990) Fiber subtype distribution of pharyngeal dilator muscles and diaphragm in the cat. *J. Appl. Physiol.* **68,** 2237–2240.

Dickersin, K. and Min, Y.I. (1993) Publication bas: the problem that won't go away. *Ann. New York Acad. Sci.* **703,** 135-146.

Ducharme, N.G. (1992) Dynamic pharyngeal collapse In: *Current therapy in equine medicine.* 3rd Ed. Ed: N.E. Robinson. WB Saunders pp 283-285.

Ducharme, N.G., Hackett, R.P., Ainsworth, D.M., Erb, H.N., and Shannon, K.J. (1994) Repeatability and normal values for measurement of pharyngeal and tracheal pressures in exercising horses. *Am. J. vet. Res.* **55,** 368-374.

Ducharme, N.G. (2001) Functional relationship of anatomy and DDSP. *J. Equine vet. Sci.* **21,** 529-532.

Ducharme, N.G., Hackett, R.P., Woodie, J.B., Dykes, N., Erb, H.N., Mitchell, L.M. and Soderholm, L.V. (2003) Investigations into the role of the thyrohyoid muscles in the pathogenesis of dorsal displacement of the soft palate in horses. *Equine vet. J.* **35,** 258-263.

Ducharme, N.G. (2006) Pharynx. In: *Equine Surgery,* 3rd Ed. Eds: J.A. Auer and J.A. Stick Saunders. pp 544-565.

Ducharme, N.G. (2008) Update on management of DDSP. Proceedings of the 14th *SIVE/FEEVA Congress.* 113-115.

Dugdale, D. and Greenwood, R. (1993) Some observations on conservative techniques for treatment of laryngopalatal displacement. *Equine vet. Educ.* **5,** 177-180.

Duncan, D. (1997) Retrospective study of 50 Thoroughbred Racehorses subjected to radical myectomy for treatment of dorsal displacement of the soft palate. *Proc. Am. Ass. equine Practnrs.* **43**, 237-238.

Durando, M.M., Martin, B.B., Hammer, E.J., Langsam, S.P., and Birks, E.K. (2002) Dynamic upper airway changes and arterial blood gas parameters during treadmill exercise. *Equine vet. J. Suppl.*, **34,** 408-412.

Durando, M.M., Martin, B.B., Davidson, E.J., and Birks, E.K. (2006). Correlations between exercising arterial blood gas values, tracheal wash findings and upper respiratory tract abnormalities in horses presented for poor performance. *Equine vet. J. Suppl*, **36,** 523-528.

Dykgraaf, S., McIlwraith, C.W., Baker, V.A., Byrd, W.J. and Daniel, R.C. (2005) Sternothyroideus tenectomy combination surgery for treatment of dorsal displacement of the soft palate in 96 Thoroughbred racehorses (1996-2004). *Proc. Am. Ass. equine Practnrs.* **51**, 323-326.

Dyson, P., Jackson, B.F., Mack, S., Pfeiffer, D.U. and Price, J.S. (2003) A study of training speeds in flat racehorses in the UK. *Proceedings of the British Equine Veterinary Association.* **42**, pp 273.

Dyson, P.K., Witte, T., Wilson, A., Jackson, B.F., Pfeiffer, D.U. and Price, J.S. (2004) Global positioning system data logging is a practical method for identifying differences in thoroughbred training regimens. *Proceedings of the British Equine Veterinary Association.* **43**, pp 204.

Dyson, S. (2011) Can lameness be graded reliably? *Equine vet. J.* **43**, 379-382.

Easterbrook, P.J., Berlin, J.A., Gopalan, R. and Matthews, D.R. (1991) Publication bias in clinical research. *Lancet.* **337**, 867-872.

Eaton, M. D. (1994) Energetics and performance. In: *The athletic horse: principles and practice of equine sports medicine.* Eds: D.R. Hodgson and R.J. Rose. Saunders. pp 49-62

Eckert, D.J., Saboisky, J.P., Jordan, A.S. and Malhotra, A. (2007) Upper airway myopathy is not important in the pathophysiology of obstructive sleep apnea. *J. Clin. Sleep Med.* **3**, 570-573.

Edstrom, L., Larsson, H. and Larsson, L. (1992) Neurogenic effects on the palatopharyngeal muscle in patients with obstructive sleep apnea. *J. Neurol. Neurosurg. Psych.* **55,** 916-920.

Ehrlich, P.J., Seeherman, H.J., Morris, E., Kolias, C., and Cook, W.R. (1995) The effect of reversible left recurrent laryngeal neuropathy on the metabolic cost of locomotion and peak aerobic power in thoroughbred racehorses. *Vet. Surg.* **24,** 36-48.

Ellis, P.D.M., Williams, J.E. and Shneerson J.M. (1993) Surgical relief of snoring due to palatal flutter: a preliminary report. *Ann. R. Coll. Surg. Eng.* **75**, 286-290.

Evans, D. (1994) Training thoroughbred racehorses. In: *The athletic horse: principles and practice of equine sports medicine.* Eds: D.R. Hodgson and R.J. Rose. Saunders. pp 393-397.

Evans, D. (2004) Exercise testing in the field. In: *Equine sports medicine and surgery* Eds: K.W. Hinchcliff, A.J. Kaneps and R.J. Geor. Saunders. pp 19-31.

Falk, G. and Fahey, T. (2009) Clinical prediction rules. *Br. Med. J.* **339**, b2899.

Fosgate, G.T. and Cohen, N.D. (2008) Epidemiological study design and the advancement of equine health. *Equine vet. J.* **40,** 693-700.

Franklin, S.H. (2002) Studies of dorsal displacement of the soft palate in thoroughbred racehorses. PhD Thesis. University of Bristol. UK.

Franklin, S.H., Naylor, J.R., and Lane, J.G. (2002a) Effect of dorsal displacement of the soft palate on ventilation and airflow during high-intensity exercise. *Equine vet. J. Suppl.*, **34,** 379-383.

Franklin, S.H., Naylor, J.R. and Lane, J.G. (2002b) The effect of a tongue-tie in horses with dorsal displacement of the soft palate. *Equine vet. J. Suppl.* **34**, 430-433.

Franklin, S.H., Price, C. and Burn, J.F. (2004) The displaced equine soft palate as a cause of abnormal respiratory noise during expiration. *Equine vet. J.* **36**, 590-594.

Franklin, S.H., Naylor, J.R. and Lane, J.G. (2006) Videoendoscopic evaluation of the upper respiratory tract in 93 sport horses during exercise testing on a high-speed treadmill. *Equine vet. J. Suppl.*, **36,** 540-545.

Franklin, S.H. and Allen, K.J. (2007) An investigation of potential associations between upper respiratory tract obstructions and lower airway inflammation. Proceedings of the 46th British Equine Veterinary Association. pp 299

Franklin, S.H. (2008) Dynamic collapse of the upper respiratory tract: A review. *Equine vet. Educ.* **20,** 212-224.

Franklin, S. (2009) Soft palate stability: Does it need more stiffness? *Proceedings of the World Equine Airways Symposium.* pp 160- 165.

Franklin, S.H., McCluskie, L.K., Woodford, N.S., Tremaine, W.H., Lane, J.G., Bladon, B.M., Barakzai, S.Z., Dixon, P.M., Hillyer, M.H. and Allen, K.J. (2009a) A comparison of the efficacy of soft palate cautery and the laryngeal tie-forward procedure in thoroughbred racehorses with a definitive diagnosis of palatal dysfunction. *Proceedings of the 48th British Equine Veterinary Association.* pp 168.

Franklin, K.A., Anttila, H., Axelsson, S., Gislason, T., Maasilta, P., Myhre, K.I. and Rehnqvist, N. (2009b) Effects and side-effects of surgery for snoring and obstructive sleep apnea-a systematic review. *Sleep.* **32,** 27-36.

Franklin, S.H., Barakzai, S.Z., Courroucé-Malblanc, A., Dixon, P., Nankervis, K.J., Perkins, J.D., Roberts, C.A., Van erck-Westergren, E. and Allen, K.J. (2010) Investigation of the incidence and type of injuries associated with high-speed treadmill exercise testing. *Equine vet. J. Suppl.* **38,** 70-75.

Garrett, K. S. (2010) How to ultrasound the larynx. *Proc. Am. Ass. equine Practnrs.* **56**, 249- 256.

Geiser, D. R. (1983) Soft palate displacement. In: *Current therapy in equine medicine.* Ed: N.E. Robinson. W.B. Saunders. pp 493-494.

Gerstenberg, C. and Dugdale, D. (1998) Transendoscopic Nd:Yag laser surgery to treat dorsal displacement of the soft palate. *Proceedings of the British Equine Veterinary Association.* **37**, 111-112.

Goldbart, A.D., Mager, E., Veling, M.C., Goldman, J.L., Kheirandish-Gozal, L., Serpero, L.D., Piedimonte, G. and Gozal, D. (2007) Neurotrophins and tonsillar hypertrophy in children with obstructive sleep apnea. *Pediatr. Res.* **62**, 489-94.

Gramkow, H.L. and Evans, D.L. (2006) Correlation of race earnings with velocity at maximal heart rate during a field exercise test in thoroughbred racehorses. *Equine vet. J. Suppl.*, **36**, 118-122.

Greenhalgh, T. (2010) How to read a paper: the basics of evidence-based medicine. 4th ed. Ed: T. Greenhalgh. Wiley-Blackwell.

Guyatt, G., Sackett, D and Haynes, B. (2006) Evaluating diagnostic tests. In: *Clinical Epidemiology: How to do clinical practice research.* 3rd Ed. Eds: R.B. Haynes, D.L. Sackett, G.H. Guyatt and P. Tugwell. Lippincott, Williams and Wilkins. pp 273-322.

Hackett, R.P., Ducharme, N.G., Fubini, S.L. and Erb, H.N. (1991) The reliability of endoscopic examination in assessment of arytenoid cartilage movement in horses. Part I: Subjective and objective laryngeal evaluation. *Vet. Surg.* **20**, 174-179.

Harrison, I.W., and Raker, C.W. (1988) Sternothyrohyoideus myectomy in horses: 17 cases (1984-1985). *J. Am. vet. med. Assoc.* **193**, 1299-1302.

Harvey, C.E. (1989) Inherited and congenital airway conditions. *J. Small animal pract.* **30**, 184-187.

Hawkes, C.S., Hahn, C.N. and Dixon, P.M. (2010) Histological and histochemical characterisation of the equine soft palate muscles. *Equine vet. J.* **42**, 431-7.

Hawkins, J.F., Tulleners E.P., Ross, M.W., Evans, L.H. and Raker, C.W. (1997) Laryngoplasty with or without ventriculectomy for treatment of left laryngeal hemiplegia in 230 racehorses. *Vet. Surg.* **26**, 484-491.

Haynes, P.F. (1981) Persistent dorsal displacement of the soft palate associated with epiglottic shortening in two horses. *J. Am. vet. med. Ass.* **179**, 677-681.

Haynes, P. F. (1983) Dorsal displacement of the soft palate and epiglottic entrapment: diagnosis, management and interrelationship. *Comp. Cont. Educ.* **5**, S379-388.

Haynes, R.B., Wilczynski, N., McKibbon, K.A., Walker, C. and Sinclair, J.C. (1994) Developing optimal search strategies for detecting clinically sound studies in Medline. *J. Med. Inform. Assoc.* **1,** 447-458.

Haynes, B. (2006a) Forming research questions In: *Clinical Epidemiology: How to do clinical practice research.* 3rd Ed. Eds: R.B. Haynes, D.L. Sackett, G.H. Guyatt and P. Tugwell. Lippincott Williams and Wilkins pp 3-14.

Haynes, B. (2006b) Conducting systematic reviews In: *Clinical Epidemiology: How to do clinical practice research.* 3rd Ed. Eds: R.B. Haynes, D.L. Sackett, G.H. Guyatt and P. Tugwell. Lippincott Williams and Wilkins pp 15-48.

Heffron, C.J., and Baker, G.J. (1979) Observations on the mechanism of functional obstruction of the nasopharyngeal airway in the horse. *Equine vet. J.* **11,** 142-147.

Hendricks, J.C. (1992) Brachycephalic airway syndrome. *Vet. Clin. N. Am.: Small Animal Pract*. **22,** 1145-1153.

Hobo, S. Matsuda, Y. and Yoshida, K. (1995) Prevalence of upper respiratory tract disorders detected with a flexible videoendoscope in thoroughbred racehorses. *J. vet. med. Sci.* **57,** 409-413.

Hogan, P.M., Palmer, S.E. and Congelosi, M. (2002) Transendoscopic laser cauterization of the soft palate as an adjunctive treatment for dorsal displacement in the racehorse. *Proc. Am. Ass. equine Practnrs.* **48,** 228-230.

Holcombe, S.J., Beard, W.L., Hinchcliff, K.W. and Robertson, J.T. (1994) Effect of sternothyrohyoid myectomy on upper airway mechanics in normal horses. *J. Appl. Physiol.* **77,** 2812-2816.

Holcombe, S.J., Derksen, F.J., Stick, J.A., Robinson, N.E., and Boehler, D.A. (1996) Effect of nasal occlusion on tracheal and pharyngeal pressures in horses. *Am. J. vet. Res.* **57,** 1258-1260.

Holcombe, S.J., Derksen, F.J., Stick, J.A. and Robinson, N.E. (1997a) Effect of bilateral tenectomy of the tensor veli palatini muscle on soft palate function in horses. *Am. J. vet. Res.* **58,** 317-321.

Holcombe, S.J., Derksen, F.J., Stick, J.A. and Robinson, N.E. (1997b) Effects of bilateral hypoglossal and glossopharyngeal nerve blocks on epiglottic and soft palate position in exercising horses. *Am. J. vet. Res.* **58,** 1022-1026.

Holcombe, S.J., Derksen, F.J., Stick, J.A. and Robinson, N.E. (1998) Effect of bilateral blockade of the pharyngeal branch of the vagus nerve on soft palate function in horses. *Am. J. vet. Res.* **59,** 504-508.

Holcombe, S.J., Derksen, F.J., Berney, C., Becker, A.C., and Horner, N.T. (2001) Effect of topical anesthesia of the laryngeal mucosa on upper airway mechanics in exercising horses. *Am. J. vet. res.* **62,** 1706-1710.

Holcombe, S.J., Cornelisse, C.J., Berney, C. and Robinson, N.E. (2002) Electromyographic activity of the hyoepiglotticus muscle and control of epiglottis position in horses. *Am. J. vet. Res.* **63**, 1617-1621.

Holcombe, S.J. and Ducharme, N.G. (2004) Abnormalities of the upper airway. In: *Equine Sports Medicine and Surgery: Basic and clinical sciences of the equine athlete.* Eds: K.W. Hinchcliff, A.J. Kaneps and R.J. Geor. Saunders. pp 559-598.

Holcombe S.J. (2006) Upper airway anatomy and physiology gone wrong: how do we diagnose the problem and what can we fix? 8th annual resort symposium of the AAEP. www.ivis.org.

Holcombe, S.J. and Ducharme, N.G. (2007) Disorders of the Nasopharynx and Soft Palate. *In: Equine Respiratory Medicine and Surgery.* Eds: B.C. McGorum, P.M. Dixon, N.E. Robinson and J. Schumacher. Saunders pp 437-457.

Holcombe, S.J., Derksen, F.J. and Robinson, N.E. (2007) Electromyographic activity of the palatinus and palatopharyngeus muscles in exercising horses. *Equine vet. J.* **39**, 451-455.

Honjo, I., Okazaki, N., and Nozoe, T. (1979) Role of the tensor veli palatini muscle in movement of the soft palate. *Acta Otolaryngol.* **88**, 137-141.

How, S.C., McConnell, A.K., Taylor, B.J. and Romer, L.M. (2007) Acute and chronic responses of the upper airway to inspiratory loading in healthy awake humans: an MRI study. *Respir. Physiol. Neurobiol.* **157**, 270-280.

Innes, J.F. (2007) Outcome-Based Medicine in Veterinary Surgery: Levels of Evidence. *Vet. Surg.* **36**, 610-612.

Isgren, C.M., Upjohn, M.M., Fernandez-Fuente, M., Massey, C., Pollot, G., Verheyen, K.L. and Piercy, R.J. (2010) Epidemiology of exertional rhabdomyolysis susceptibility in standardbred horses reveals associated risk factors and underlying enhanced performance. *Plos One*, **5**, e11594.

Jager-Hauer, K., Lutkefels, E., Deegan, E., Drommer, W., and Ohnesorge, B. (2003) Experimental study on transendoscopic laser surgery of dorsal displacement of the soft palate in horses. *Tierarztl Prax Ausg G Grosstiere Nutztiere* **31**, 18-24.

Jones, N.L., Robertson, D.G., Kane, J.W. (1979) Difference between end-tidal and arterial PCO_2 in exercise. *J. Appl. Physiol.* **47**, 954-960.

Jordan, A.S., and White, D.P. (2008) Pharyngeal motor control and the pathogenesis of obstructive sleep apnea. *Respir. Physiol. Neurobiol.* **160**, 1-7.

Jose-Cunilleras, E., Young, L. Newton, J.R. and Marlin, D.J. (2006) Cardiac arrhythmias during and after treadmill exercise in poorly performing Thoroughbred racehorses. *Equine vet. J. Suppl.* **36**, 163-170.

Kannegieter, N.J. and Dore, M.L. (1995) Endoscopy of the upper respiratory tract during treadmill exercise: a clinical study of 100 horses. *Aust. vet. J.* **72**, 101-107.

Kastner, S.B.R., Weishaupt, M.A. and Townsend, H.G.G., 1998. Evaluation of the upper respiratory tract in the horse during treadmill exercise – a revew. Part II: Measurement of upper airway flow mechanics. *Pferdeheilk*, **14**, 33–40.

Kimoff, R.J. (2007) Upper airway myopathy is important in the pathophysiology of obstructive sleep apnea. *J. clin. sleep med.* **3**, 567-569.

King, D.S., Tulleners, E., Martin, B.B., Jr., Parente, E.J. and Boston, R. (2001) Clinical experiences with axial deviation of the aryepiglottic folds in 52 racehorses. *Vet. Surg.* **30**, 151-160.

Koch, C. (1991) Augmentation of the equine epiglottis with Teflon paste. *Proc. Am. Ass. Equine Practnrs.* **36**, 541-545.

Kogo, M., Tanaka, S., Ishii, S., Hamaguchi, M., Iida, S. and Matsuya, T. (1997) Activities of superior pharyngeal constrictor and levator veli palatini muscles related to respiration in dogs. *Cleft Palate Craniofac. J.* **34**, 338-341.

Kuna, S. and Vanoye, C. (1999) Mechanical effects of pharyngeal constrictor activation on pharyngeal airway function. *J. Appl. Physiol.* **86**, 411-417.

Kuhle, S. and Urschitz, M.S. (2011) Anti-inflammatory medications for obstructive sleep apnea in children. *Cochrane Database Syst. Rev.* **1**, CD007074.

Kwon, T.K. and Buckmire, R. (2004) Injection laryngoplasty for management of unilateral vocal fold paralysis. *Curr. Opin. Otolaryngol. Head Neck Surg.* **12**, 538-542.

Lafrentz, J.R., Brietzke, S.E. and Mair, E.A. (2003) Evaluation of palatal snoring surgery in an animal model. *Otolaryngol. Head Neck Surg.* **129**, 343-352.

Lane, J.G. (1993) Dorsal displacement of the soft palate, epiglottic entrapment and related conditions. In: *Proceedings of the Bain-Fallon Memorial Lectures*, Queensland, Australia, pp. 193–206.

Lane, J.G., Bladon, B., Little, D.R., Naylor, J.R. and Franklin, S.H. (2006a) Dynamic obstructions of the equine upper respiratory tract. Part 1: observations during high-speed treadmill endoscopy of 600 Thoroughbred racehorses. *Equine vet. J.* **38**, 393-399.

Lane, J.G., Bladon, B., Little, D.R., Naylor, J.R. and Franklin, S.H. (2006b) Dynamic obstructions of the equine upper respiratory tract. Part 2: comparison of endoscopic findings at rest and during high-speed treadmill exercise of 600 Thoroughbred racehorses. *Equine vet. J.* **38**, 401-407.

Leprêtre, P-M., Metayer, N., Giovagnoli, G., Pagliei, E. and Barrey, E. (2009) Comparison of analyses of respiratory gases made with the K4b2 portable and Quark laboratory analysers in horses *Vet. Rec.* **165**, 22-25.

Lindman, R. and Stahl, P.S. (2002) Abnormal palatopharyngeal muscle morphology in sleep-disordered breathing. *J. Neurol. Sci.* **195**, 11-23.

Lindner, A.E. (2009) Relationships between racing times of Standardbreds and v4 and v200. *J. Anim. Sci.* **88**, 950-954.

Linford, R.L., O'Brien, T.R., Wheat, J.D. and Meagher, D.M. (1983) Radiographic assessment of epiglottic length and pharyngeal and laryngeal diameters in the Thoroughbred. *Am. J. vet. Res.* **44**, 1660-1666.

Llewellyn, H.R. and Petrowitz, A.B. (1997) Sternothyroideus myotomy for treatment of dorsal displacement of the soft palate. *Proc. Am. Ass. equine Practnrs.* **43**, 239-243.

Lumsden, J.M., Brown, C.M., Stick, J.A., Godber, L.M., Caron, J.J., Derksen, F.J., and Nickels, F.A. (1995) Upper airway function in performance horses: videoendoscopy during high-speed treadmill exercise. *Comp. cont. Educ. Pract. Vet.* **17**, 1134-1143.

Main, C., Liu, Z., Welch, K., Weiner, G., Jones, S.Q. and Stein, K. (2009) Surgical procedures and non-surgical devices for the management of non-apnoeic snoring: a systematic review of clinical effects and associated treatment costs. *Health Technol. Assess.***13**, 1-208.

Marcoux, M., Picandet, V., Celeste, C., Macieira, S., Morisset, S., Rossier, Y., Schambourg, M. and Jean, D. (2008) Palatal sclerotherapy: a potentially useful treatment of intermittent dorsal displacement of the soft palate in juvenile standardbred racehorses. *Can. vet. J.* **49**, 587-591.

Marlin, D.J., Roberts, C.A., Schroter, R.C. and Lekeux, P. (2000) Respiratory responses of mature horses to intravenous lobeline bolus. *Equine vet. J.* **32**, 200-207.

Martin, G.S., Strand, E. and Kearney, M.T. (1996) Use of statistical models to evaluated racing performance in Thoroughbreds. *J. Am. vet. med. Ass.* **209**, 1900-1906.

Martin, B.B., Jr., Reef, V.B., Parente, E.J. and Sage, A.D. (2000) Causes of poor performance of horses during training, racing, or showing: 348 cases (1992-1996). *J. Am. vet. med. Ass.* **216**, 554-558.

McCann, J. (2000) Differential diagnosis of abnormal respiratory noises in the exercising horse. *In Prac.* **22**, 370-381.

McCluskie, L.K., Merriam, A.G. and Franklin, S.H. (2006) A histological examination of the equine aryepiglottal folds. In: *Proceedings of the 45th BEVA Congress.* Equine Veterinary Journal Ltd, Newmarket. p 322.

McCluskie L.K., Franklin S.H., Lane J.G., Tremaine W.H. and Allen K.J. (2008) Effect of head position on radiographic assessment of laryngeal tie-forward procedure in horses. *Vet. Surg.* **37**, 608-12.

McCluskie, L.K., Franklin, S.H., Tremaine, W.H., Woodford, N.S. and Allen, K.J. (2009) Post-operative high speed treadmill endoscopy to determine the efficacy of upper respiratory tract surgery in horses with palatal dysfunction. *Proceedings of the 48th British Equine Veterinary Association* pp 168.

McWhorter, A.J., Rowley, J.A., Eisele, D.W., Smith, P.L., and Schwartz, A.R. (1999) The effect of tensor veli palatini stimulation on upper airway patency. *Arch. Otolaryngol. Head Neck Surg.* **125**, 937-940.

Meakins, J.L. (2002) Innovation in surgery: the rules of evidence. *Am. J. Surg.* **183**, 399-405.

Midgley, A.W., McNaughton, L.R. and Carroll, S. (2007) Physiological determinants of time to exhaustion during intermittent treadmill running at vVO_{2max}. *Int. J. Sports Med.* **28**, 273-280.

Mitchinson, A.G. and Yoffrey, J.M. (1947) Respiratory displacement of larynx, hyoid bone and tongue. *J. Anat.* **81**, 118-121.

Moher, D., Jadad, A.R., Nichol, G. Penman, M., Tugwell, P. and Walsh, S. (1995) Assessing the quality of randomised controlled trials: an annotated bibliography of scales and checklists. *Controlled Clin. Trials* **16**, 62-73.

Moon, J.B., Thompson, S.A., Jaeckel, E. and Canady, J.W. (1998) Muscle fiber type distribution in the normal human levator veli palatini muscle. *Cleft Palate Craniofac. J.* **35**, 419-424.

Morello, S.L., Ducharme, N.G., Hackett, R.P., Warnick, L.D., Mitchell, L.M. and Soderholm, L.V. (2008) Activity of selected rostral and caudal hyoid muscles in clinically normal horses during strenuous exercise. *Am. J. vet. Res.* **69**, 682-689.

Morris, E.A. and Seeherman, H.J. (1990) Evaluation of upper respiratory tract function during strenuous exercise in racehorses. *J. Am. vet. med. Ass.* **196**, 431-438.

Morris, E.A. and Seeherman, H.J. (1991) Clinical evaluation of poor performance in the racehorse: the results of 275 evaluations. *Equine vet. J.* **23**, 169-174.

Muñoz, J.A., Marcoux, M., Picandet, V., Theoret, C.L., Perron, M.F. and Lepage, O.M. (2010) Histological and biomechanical effects of palatal sclerotherapy in the horse using sodium tetradecyl sulfate. *Vet. J.* **183**, 316-321.

Murphy, S.A. (2002) Applying methodological search filters to CAB Abstracts to identify research for evidence-based veterinary medicine. *J. Med. Lib. Assoc.* **90**, 406-410.

Murphy, S.A. (2003) Research methodology search filters are they effective for locating research for evidence based veterinary medicine in PubMed? *J. Med. Lib. Assoc.* **91**, 484-489.

Negus, V.E. (1929) The function of the epiglottis *J. Anat.* **62**, 1-8.

Newcombe, R.G. (1987) Towards a reduction in publication bias. *Br. Med. J. (Clin. Res. Ed.)* **295**, 656-659.

Nuttal, T. and Cole, L.K. (2007) Evidence-based veterinary dermatology: a systematic review of interventions for treatments of Pseudomonas otitis in dogs. *Vet. Derm.* **18**, 69-77.

Ohnesorge, B., and Deegen, E. (1998) Transendoscopic laser surgery of exercise-induced dorsal displacement of the soft palate in horses. *Tierarztl Prax Ausg G Grosstiere Nutztiere* **26**, 287-293.

Oliven, A., Odeh, M., Geitini, L., Oliven, R., Steinfeld, U., Schwartz, A.R. and Tov, N. (2007) Effect of coactivation of tongue protrusor and retractor muscles on pharyngeal lumen and airflow in sleep apnea patients. *J. Appl. Physiol.* **103**, 1662-1668.

Olivry, T. and Mueller, R.S. (2003) Evidence- based veterinary dermatology: a systematic review of the pharmacotherapy of canine atopic dermatitis. *Vet. Derm.* **14**, 121-146.

O'Meara, B., Bladon, B., Parkin, T.D., Fraser, B. and Lischer, C.J. (2010) An investigation of the relationship between race performance and superficial digital flexor tendonitis in the Thoroughbred racehorse. *Equine vet. J.* **42,** 322-326.

O'Rielly, J.L., Beard, W.L., Renn, T.N., Padden, A.J., and Hinchcliff, K.W. (1997) Effect of combined staphylectomy and laryngotomy on upper airway mechanics in clinically normal horses. *Am. J. vet. res.* **58,** 1018-1021.

Ordidge, R. (2001) The treatment of dorsal displacement of the soft palate by thermal cautery: A review of 252 cases. *Proceedings of the 2nd World Equine Airways Symposium.*

Parente, E.J., Martin, B.B., Tulleners, E.P. and Ross, M.W. (1994) Upper respiratory dysfunctions in the horse during high-speed exercise. *Proc. Am. Ass. equine Practnrs.* **40,** 81-82.

Parente, E.J. and Martin, B.B. (1995) Correlation between standing endoscopic examinations and those made during high-speed exercise in horses - 150 cases. *Proc. Am. Ass. equine Practnrs* **41,** 170.

Parente, E.J. (1996) Testing methods for exercise intolerance in horses. *Vet. Clin. N. Am.: Equine Prac.* **12,** 421-433.

Parente, E.J. (1997) Treadmill endoscopy. *In: Equine Endoscopy 2nd Edition* Eds: C.M. Brown and J.L. Traub-Dargatz. Mosby St Louis pp 102-116.

Parente, E.J. (1998) Value of high-speed treadmill endoscopy. *Proc. Am. Ass. equine Practnrs.* **44,** 30-33.

Parente, E.J., Martin, B.B., Tulleners, E.P. and Ross, M.W. (2002) Dorsal displacement of the soft palate in 92 horses during high-speed treadmill examination (1993-1998). *Vet. Surg.* **31**, 507-512.

Parente, E.J. and Derksen, F.J. (2006) Diagnostic techniques in equine upper respiratory tract disease. In: *Equine Surgery.* 3rd Ed. Eds: J.A. Auer and J.A. Stick. pp 522-533.

Parente, E.J., Tulleners, E.P. and Southwood, L.L. (2008) Long-term study of partial arytenoidectomy with primary mucosal closure in 76 Thoroughbred racehorses (1992-2006). *Equine vet. J.* **40,** 214-218.

Parkin, T. D. H. (2008) Epidemiology of racetrack injuries in racehorses. *Vet. Clin. N. Am.: Equine Prac.* **24,** 1-19.

Peloso, J.G., Stick, J.A., Nickels, F.A., Lumsden, J.M. and Derksen, F.J. (1992) Epiglottic augmentation by use of polytetrafluoroethylene to correct dorsal displacement of the soft palate in a standardbred horse. *J. Am. vet. med. Ass.* **201**, 1393-1395.

Perkins, J.D., Salz, R.O., Schumacher, J., Livesey, L., Piercy, R.J. and Barakzai, S.Z. (2009) Variability of resting endoscopic grading for assessment of recurrent laryngeal neuropathy in horses. *Equine vet J.* **41**, 342-346.

Petrie, A. and Sabin, C. (2005) Diagnostic tools. In: *Medical statistics at a glance*. 2nd Ed. Eds: A. Petrie and C. Sabin. pp 102-103.

Petrof, B.J., Pack, A.I., Kelly, A.M., Eby, J. and Hendricks, J.C. (1994) Pharyngeal myopathy of loaded upper airway in dogs with sleep apnea. *J Appl. Physiol.* **76**, 1746-1752.

Picandet, V., Marcoux, M., Jean, D., Celeste, C., Macieira, S., Morisset, S. and Schambourg, M. (2005) Palatal sclerotherapy for the treatment of intermittent dorsal displacement of the soft palate in 50 standardbred racehorses. *Proceedings of the 3rd World Equine Airways Symposium.* pp 128.

Pierce, R. and Worsnop, C. (1999) Upper airway function and dysfunction in respiration. *Clin. Exp. Pharmacol. Physiol.* **26**, 1-10.

Pigott, J.H., Ducharme, N.G., Mitchell, L.M., Soderholm, L.V. and Cheetham, J. (2010) Incidence of swallowing during exercise in horses with dorsal displacement of the soft palate. *Equine vet. J.* **42,** 732-737.

Pollock, P.J. and Reardon, R.J.M. (2009) Dynamic respiratory endoscopy without a treadmill: Initial experiences. *Equine vet. Educ.* **21**, 367-370.

Pollock, P.J., Reardon, R.J.M., Parkin, T.D.H., Johnston, M.S., Tate, J. and Love, S. (2009) Dynamic respiratory endoscopy in 67 Thoroughbred racehorses training under normal ridden exercise conditions. *Equine vet. J.* **41,** 354-360.

Popay, J., Roberts, H., Sowden, A., Petticrew M., Arai, L., Rodgers, M., Britten N., Roen K. and Duffy, S. (2006) Guidance on the conduct of narrative synthesis in systematic reviews. Institute for health research, University of Lancaster.

Poyrazoglu, E, Dogru, S, Saat, B, Güngör, A, Cekin, E and Cincik, H. (2006) Histologic effects of injection snoreplasty and radiofrequency in the rat soft palate. *Otolaryngol. Head Neck Surg.* **135**, 561-564.

Quinlan, J., Van Rensburg, S.W.J. and Starke, N.C. (1949) The soft palate (*Palatinum Molle*) as a cause of dyspnoea in two racehorses. *J. South Africa vet. med. Assoc.* **20,** 125-127.

Reardon, R.J., Fraser, B.S., Heller, J., Lischer, C., Parkin, T. and Bladon, B.M. (2008a) The use of race winnings, ratings and a performance index to assess the effect of thermocautery of the soft palate for treatment of horses with suspected intermittent dorsal displacement. A case-control study in 110 racing Thoroughbreds. *Equine vet. J.* **40**, 508-513.

Reardon, R.J.M., Fraser, B.S.L. and Bladon, B.M. (2008b) Laryngeal tie-forward combined with thermocautery as treatment of horses with signs associated with intermittent dorsal displacement of the soft palate: A case-control study in British racing Thoroughbreds. *Proceedings of the 47th British Equine Veterinary Association* pp 340.

Reeves, B.C., Deeks J.J, Higgins J.P.T., Wells G.A. (2008) Chapter 13: Including non-randomized studies. In: *Cochrane Handbook for systematic reviews of interventions* Version 5. Eds: J.P.T. Higgins and S. Green. The Cochrane Collaboration (www.cochrane-handbook.org).

Rehder, R.S. (1992) Measurement of upper airway pressures in exercising horses: effects of speed, workload, fasting and presence of the endoscope. MS Thesis. Cornell University. pp 73-99.

Rehder, R.S., Ducharme, N.G., Hackett, R.P., and Nielan, G.J. (1995) Measurement of upper airway pressures in exercising horses with dorsal displacement of the soft palate. *Am. J. vet. Res.* **56,** 269-274.

Richardson, L.E., Wakley, G.K. and Franklin, S.H. (2006) A quantitative study of the equine soft palate using histomorphometry *Vet. J.* **172**, 78-85.

Riley, R.W., Powell, N.B. and Guilleminault, C. (1989) Inferior mandibular osteotomy and hyoid myotomy suspension for obstructive sleep apnea: a review of 55 patients. *Oral Maxillofac. Surg.* **47,** 159-164.

Riley, R.W., Powell, N.B. and Guilleminault, C. (1994) Obstructive sleep apnea and the hyoid: a revised surgical procedure. *Otolaryngol. Head Neck Surg.* **111**, 717-721.

Roberts, J.L., Reed, W.R. and Thach, B.T. (1984) Pharyngeal airway-stabilizing function of sternohyoid and sternothyroid muscles in the rabbit. *J. Appl. Physiol.* **57**, 1790-1795.

Rodenstein, D.O. and Stănescu, D.C. (1984) *Soft palate and oronasal breathing in humans. J. Appl. Physiol.* **57**, 651-657.

Romer, L.M. and Polkey, M.I. (2008) Exercise-induced respiratory muscle fatigue: Implications for performance. *J. Appl. Physiol.* **104**, 879-888.

Roneus, B., Andersson, A.M. and Ekman, S. (1997) Racing performance in standardbred trotters with chronic synovitis after partial arthroscopic synovectomy in the metacarpophalangeal, metatarsophalangeal and intercarpal (midcarpal) joints. *Acta vet. Scand.* **38,** 87-95.

Rose, R.J. and Hodgson, D.R. (1994) Clinical exercise testing. In: *The athletic horse: principles and practice of equine sports medicine.* Eds: D.R. Hodgson and R.J. Rose. Saunders. pp 245-257.

Rothstein, R.J., Narce, S.L., Dewberry-Borowiecki, B. and Blanks, R.H.I. (1983) Respiratory-related activity of upper airway muscles in anesthetized rabbit. *J. Appl. Physiol.* **55**, 1830-1836.

Sackett, D.L., Rosenberg, W.C. and Gray, J.A.M. (1996) Evidence based medicine: what it is and what it isn't. *Br. Med. J.* **312**, 71-72.

Sackett, D.L., Straus, S.E., Richardson, W.S., Rosenberg, W. and Haynes, R.B. (2000) Evidence based medicine: How to practice and teach EBM. Churchill Livingston pp 1-12.

Saulez, M.N. and Gummow, B. (2009) Prevalence of pharyngeal, laryngeal and tracheal disorders in thoroughbred racehorses and effect on performance. *Vet. Rec.* **165,** 431-435.

Schroter, R. C. and Marlin, D.J. (2002) Modelling the oxygen cost of transport in competitions over ground of variable slope. *Equine vet. J. Suppl.* **34,** 397-401.

Seeherman, H.J., Morris, E. and O'Callaghan, M.W. (1992) Comprehensive clinical evaluation of performance. In: Equine surgery. Ed: J.A. Auer. Saunders. pp 1153-1155.

Series, F.J., Simoneau, S.A., St Pierre, S. and Marc, I. (1996) Characteristics of the genioglossus and musculus uvulae in sleep apnea hypopnea syndrome and in snorers. *Am. J. Respir. Crit. Care Med.* **153**, 1870-1874.

Series, F., Cote, C. and St Pierre, S. (1999) Dysfunctional mechanical coupling of upper airway tissues in sleep apnea syndrome. *Am. J. Respir. Crit. care med.* **159**, 1551-1555.

Series, F. (2002) Upper airway muscles awake and asleep. *Sleep Medicine Reviews* **6,** 229-242.

Sheldon, T. (2005) Making evidence synthesis more useful for management and policy making. *J. Health Serv. Res. Policy* **10** (suppl 1) 1-5.

Shneerson, J. and Wright, J. (2001) Lifestyle modification for obstructive sleep apnoea. *Cochrane Database Syst. Rev.* CD002875.

Sisson, S. (1975) Equine Myology. *In: The Anatomy of the Domestic Animals* 5th Ed. Eds: S.Sisson and J.D. Grossman. WB Saunders. pp 376-453.

Sisson, S. and Grossman, J.D. (1953) *The Anatomy of the Domestic Animals*, 4th edn., W.B. Saunders, London. pp 407-410.

Slocombe, R., Brock, K., Covelli, G. and Bayly, W. (1991) Effect of treadmill exercise on intrapleural, transdiaphragmatic and intra-abdominal pressures in Standardbred horses. In: *Equine Exercise Physiology*, 3rd Ed. Eds: S.G.B. Persson, A. Lindholm, L.B. Jeffcott, ICEEP Publications, Davis, CA. pp 83-91.

Sloet van Oldruitenborgh-Oosterbaan, M.M. and Barneveld, A. (1995) Comparison of the workload of Dutch warmblood horses ridden normally and on a treadmill. *Vet. Rec.* **137**, 136-9.

Sloet van Oldruitenborgh-Oosterbaan, M.M. and Clayton, H.M. (1999) Advantages and disadvantages of track vs. treadmill tests. *Equine vet. J. Suppl.* **30**, 645-647.

Smith, J.J. and Embertson, R.M. (2005) Sternothyroideus myotomy, staphylectomy, and oral caudal soft palate photothermoplasty for treatment of dorsal displacement of the soft palate in 102 thoroughbred racehorses. *Vet. Surg.* **34**, 5-10.

Smith, I., Lasserson, T.J. and Wright, J. (2006) Drug therapy for obstructive sleep apnoea in adults. *Cochrane Database Syst. Rev.* **19**, CD003002.

Stål, P.S. and Lindman, R. (2000) Characterisation of human soft palate muscles with respect to fibre types, myosins and capillary supply. *J. Anat.* **197**, 275-290.

Stål, P.S., Lindman, R. and Johansson, B. (2009) Capillary supply of the soft palate muscles is reduced in long-term habitual snorers. *Respir.* **77**, 303-310.

Stick, J.A., Derksen, F.J., Nickels, F.A., Brown, C.M., Arden, W.A., Fulton, I.C. and Peloso, J.G. (1990) Upper airway videoendoscopy during exercise in poorly performing horses. *Proc. Am. Ass. equine Practnrs.* **36**, 431-438.

Strand, E., Hanche-Olsen, S. and Fjordbakk, C. (2009) Complex dynamic upper airway collapse: Relationships between diagnosis in 99 Harness racehorses with one or more concurrent dynamic abnormalities. *Proceedings of the 4th World Equine Airways Symposium.* pp 248.

Stroup, D.F., Berlin, J.A., Morton, S.C., Olkin, I., Williamson, G.D., Rennie, D., Moher, D., Becker, B.J., Sipe, T.A. and Thacker, S.B. (2000) Meta-analysis of observational studies in epidemiology: A proposal for reporting. *J. Am. Med. Assoc.* **283**, 2008-2012.

Sundaram, S., Bridgman, S.A., Lim, J. and Lasserson, T.J. (2005) Surgery for obstructive sleep apnoea. *Cochrane Database Syst. Rev.* **19**, CD001004.

Svanborg, E. (2005) Impact of obstructive apnea syndrome on upper airway respiratory muscles. *Respir. Physiol. Neurobiol.* **147**, 263-272.

Tan, R.H., Dowling, B.A. and Dart, A.J. (2005) High-speed treadmill videoendoscopic examination of the upper respiratory tract in the horse: the results of 291 clinical cases. *Vet. J.* **170**, 243-248.

Tangel, D.J., Mezzanotte, W.S. and White, D.S. (1995) Respiratory-related control of palatoglossus and levator palatini muscle activity. *J. Appl. Physiol.* **78**, 680-688.

Taylor, S.E., Barakzai, S.Z. and Dixon, P. (2006) Ventriculocordectomy as the sole treatment for recurrent laryngeal neuropathy: long-term results from ninety-two horses. *Vet. Surg.* **35**, 653-657.

Tessier, C., Holcombe, S.J., Stick, J.A., Derksen, F.J. and Boruta, D. (2005) Electromyographic activity of the stylopharyngeus muscle in exercising horses. *Equine vet. J.* **37**, 232-235.

Tsukroff, E., Ducharme, N.G., Bertram, J. and Hackett, R.P. (1998) Relationship of basihyoid bone and thyroid cartilage in exercising horses. *Proceedings of the first world equine airways symposium.*

Tulleners, E., Mann, P. and Raker, C.W. (1990) Epiglottic augmentation in the horse. *Vet. Surg.* **19**, 181-190.

Tulleners, E.P. and Hamir, A. (1991) Evaluation of epiglottic augmentation by use of polytetrafluoroethylene paste in horses. *Am. J. vet. res.* **52**, 1908-1916.

Tulleners, E.P. (1995) Surgical management of DDSP. In: *Proceedings of the 23rd annual surgical forum,* Chicago. pp 141-145.

Tulleners, E. Stick, J.A., Leitch, M., Trumble, T. and Wilkerson, J.P. (1997) Epiglottic augmentation for treatment of dorsal displacement of the soft palate in racehorses: 59 cases (1985-1994). *J. Am. vet. med. Ass.* **211,** 1022-1028.

Van de Graaff, W., Gottfried, S.B, Mitra, J., van Lunteren, E., Cherniack, N.S, and Strohl, K.P (1984) Respiratory function of hyoid muscles and hyoid arch. *J. Appl. Physiol.* **57**, 197-204.

Van de Graaff, W.B. (1988) Thoracic influence on upper airway patency. *J. Appl. Physiol.* **65,** 2124-2131.

Van der Touw, T., O'Neill, N., Brancatisano, A., Amis, T., Wheatley, J. and Engel, L. (1994a) Respiratory-related activity of soft palate muscles: augmentation by negative upper airway pressure. *J. Appl. Physiol.* **76**, 424-432.

Van der Touw, T., O'Neill, N., Amis, T., Wheatley, J. and Brancatisano, A. (1994b) Soft palate muscle activity in response to hypoxic hypercapnia. *J. Appl. Physiol.* **77**, 2600-2605.

Van Erck-Westergren E., Frippiat T., Dupuis M.C., Richard E., Art T. and Desmaizieres L.M. (2009) Upper airway dynamic endoscopy: Are track and treadmill observations comparable? *Proceedings of the 4th World Equine Airways Symposium* pp 254-255.

Van Lunteren, E. (1990) Role of mammalian hyoid muscles in the maintenance of pharyngeal patency. *Sleep respir.* **345**, 125-136.

Van Lunteren, E., Salomone, R.J., Manubay, P., Supinski, G.S. and Dick, E. (1990) Contractile and endurance properties of geniohyoid and diaphragm muscles. *J. Appl. Physiol.* **69**, 1992–1997.

Van Lunteren, E. (1993) Muscles of the pharynx: structural and contractile properties. *Ear Nose Throat J.* **72**, 2733-2739.

Vermeulen, A.D. and Evans, D.L. (2006) Measurements of fitness in thoroughbred racehorses using field studies of heart rate and velocity with a global positioning system. *Equine vet. J. Suppl.*, **36,** 113-117.

Vieira, B.B., Itikawa, C.E., de Almeida, L.A., Sander, H.S., Fernandes, R.M., Anselmo-Lima, W.T. and Valera, F.C. (2011) Cephalometric evaluation of facial pattern and hyoid bone position in children with obstructive sleep apnea syndrome. *Int. J. Pediatr. Otorhinolaryngol.* **75,** 383-386.

Vincent, H.K., Shanely, R.A., Stewart, D.J., Demirel, H.A., Hamilton, K.L., Ray, A.D., Michlin, C., Farkas, G.A. and Powers, S.K. (2002) Adaptation of upper airway muscles to chronic endurance exercise. *Am. J. Respir. Crit. Care Med.* **166**, 287-293.

Vincent, T.L., Newton, J.R., Deaton, C.M., Franklin, S.H., Biddick, T., McKeever, K.H., McDonough, P., Young, L.E., Hodsgon, D.R. and Marlin, D.J. (2006) Retrospective study of predictive variables for maximal heart rate in horses undergoing strenuous treadmill exercise. *Equine vet. J. Suppl* **36**, 146-152.

Wagner, P.D., Gillespie, J.R., Landgren, G.L., Fedde, M.R., Jones, B.W., DeBowes, R.M., Pieschl, R.L., Erickson, H.H. (1989) Mechanism of exercise-induced hypoxemia in horses. *J. Appl. Physiol.* **66**, 1227-1233.

Wang, Z., Rebeiz, E.E. and Shapsay, S.M. (2002) Laser soft palate 'stiffening': an alternative to uvulopalatopharyngoplasty. *Lasers surg. med.* **30**, 40-43.

Wassmuth, Z., Mair, E., Loube, D. and Leonard, D. (2000) Cautery-assisted palatal stiffening operation for the treatment of obstructive sleep apnea syndrome. *Otolaryngol. Head Neck Surg.* **123**, 55-60.

Weishaupt, M.A., Kastner, S.B.R., Grieshaber, K. and K., v.P. (1998) Airflow limitations in laryngeal hemiplegia: chemical versus exercise induced hyperventilation. *Proceedings of the first world equine airways symposium.* pp 9.

Weishaupt, M.A. (2005) Upper airway mechanics. *Proceedings of the 3rd world equine airways symposium.* pp 85-94.

Wiegand, D.A. and Latz, B. (1991) Effect of geniohyoid and sternohyoid muscle contraction on upper airway resistance in the cat. *J. Appl. Physiol.* **71**, 1346 -1354

Witte, S.H.P., Witte, T.H., Harriss, F., Kelly, G. and Pollock, P. (2011) Association of owner-reported noise with findings during dynamic respiratory endoscopy in Thoroughbred racehorses. *Equine vet. J.* **43**, 9-17.

Woodie, J.B., Ducharme, N.G., Kanter, P., Hackett, R.P. and Erb, H.N. (2005a) Surgical advancement of the larynx (laryngeal tie-forward) as a treatment for dorsal displacement of the soft palate in horses: a prospective study 2001-2004. *Equine vet. J.* **37**, 418-423.

Woodie, J.B., Ducharme, N.G., Hackett, R.P., Erb, H.N., Mitchell, L.M. and Soderholm, L.V. (2005b) Can an external device prevent dorsal displacement of the soft palate during strenuous exercise? *Equine vet. J.* **37**, 425-429.

Woodson, B.T., Garancis, J.C. and Toohill, R.J. (1991) Histopathologic changes in snoring and obstructive sleep apnea syndrome. *Laryngoscope.* **101**, 1318-22.

Wykes, P.M. (1991) Brachycephalic airway obstructive syndrome. *Problems in veterinary medicine.* **3**, 188-197.

Young, L.E., Rogers, K. and Wood J.L. (2008) Heart murmurs and valvular regurgitation in thoroughbred racehorses: epidemiology and associations with athletic performance. *J. vet. Intern. Med.* **22**, 418-426.

Appendix I: Methodological assessment checklist for studies investigating the effect of an intervention for equine dynamic upper respiratory tract disorders.

Criteria	Answer
Study design	
Was a comparison group used?	Yes No
Is the comparison/control group appropriate?	Yes appropriate Somewhat likely to be biased Highly likely to be biased
Are the inclusion criteria clearly defined by the authors?	Adequate Inadequate
Are adequate baseline details presented?	Adequate Inadequate
If a comparison group is included, are the groups comparable at baseline?	Yes No Unsure Not applicable
Is there likely to be a systematic difference between groups (i.e. other than the factor of interest)	Yes No Unsure Not applicable
Are potential confounders identified and controlled for?	Yes No
Was a power calculation performed?	Yes No
Is sample size likely to be sufficient to detect a clinically relevant effect?	Yes No Unsure
Are greater than 80% included in follow up?	Yes No
Were reasons for each exclusion explicitly explained?	Yes No
Was a definitive diagnosis established in all cases?	Yes No
Is case definition sufficiently explicit to exclude similar conditions?	Yes No
Was there a clear description of the intervention?	Yes No
Was the intervention standardised between cases?	Yes No Unsure
Is there evidence that the intended intervention and only that intervention was experienced by all of the	Yes No

horses in the treatment group? (and not in the control group?)	Unsure
Is the outcome measure relevant and meaningful?	Yes No Unsure
Is the outcome measure clearly defined?	Yes No
Were adverse effects reported?	Yes No
Are the limitations of the study discussed?	Yes No
Are the data analyses appropriate?	Yes No Unsure
Are the conclusions of the study supported by the results?	Yes No
Are the results generalisable to other populations of interest?	Yes No

Appendix II: Summary tables and data of included studies

Data for each included study, the reported success rates in the original study and the main limitations of the studies are presented in the tables below.

The data were then extracted or calculated from the original study so that further analysis could be performed in this review. The effect measures reported by the trial authors were used. In studies in which a comparison group was presented, a quantitative analysis was performed where possible and effectiveness summarised as odds ratio using 95% confidence intervals, using the Mantel-Haenszel method (Review Manager Software: www.cochrane.org/resources/handbook). The forest plots for these analyses are presented underneath the relevant table. For consistency through this review, in studies where multiple race performance analyses were undertaken, only the forest plot for the outcome measure of improved race earnings for three races before compared with three races after the intervention is shown. When the study assessed more than two treatments, all comparisons are shown. However, it should be acknowledged that undertaking multiple statistical tests might affect the type 1 error rate.

Forest plots are used to show the results of several similar studies, which can be combined to provide a single estimate of effect. As no studies in this review assessed the same intervention and comparator using the same outcome measure, it was not possible to pool the results as typically occurs in a systematic review with a meta-analysis. The forest plots are used in this systematic review to give the reader a simple graphical representation of the direction of effect. In this review no weightings were assigned to the studies, therefore the forest plots do not take into account the limitations of the study.

TB = thoroughbred, SB = standardbred, WB = warmblood. DDSP = dorsal displacement of the soft palate, PI = palatal instability.

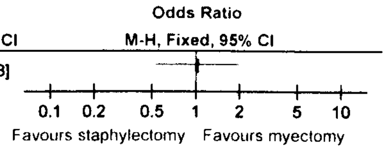
Ahern 1993b	Journal publication
Study design	Pre post (some controls reported to be assessed but results not provided)
Participants	111 racehorses underwent procedure, of which 100 (13 SB and 87 TB) (90%) were assessed by the author. 5 cases were removed from this review because of concurrent laryngoplasty.
Intervention assessed	Oral palatopharyngoplasty (Ahern procedure – elliptical oral palatine mucosal resection and sub-epiglottic mucosal resection).
Outcomes	Subjectively assessed by author. Surgical success was designated when there was marked reduction in the individual group of presenting symptoms which led to the diagnosis. Race performance was also examined; the intervention was considered unsuccessful in horses that performed at the same level or lower post-operatively.
Reported success of procedure	Intervention considered successful in 70/95 (74%).

Adverse effects	Not reported
Main study limitations	Definitive diagnosis not achieved No comparison group Subjectively assessed, outcome measure not clearly defined and varied between horses. No details presented on numbers of controls (these had equivalent diagnosis but not surgery) or the results of these. Probable variation in surgical technique (such as length, width, depth and position of the rostral palate surgery and different suture materials used Ahern (1993a)). Adverse effects not reported

Anderson *et al.* 1995	Journal publication
Study design	Parallel group pre post
Participants	209 (83 SB and 126 TB) racehorses underwent either procedure, of which 149 (71%) were assessed.
Interventions assessed	Sternothyrohyoideus myectomy (SM) (n=80) versus Staphylectomy (S) (n=69)
Outcomes	Objective assessment determined by race earnings (3 races after intervention compared with 3 races before intervention). Subjective assessment by owner attempted in 60 horses for which race records were unavailable, but only obtained for 9.
Reported success of procedure	Reported success rate of 60% for sternothyrohyoideus myectomy and 59% for staphylectomy. (Comparisons between interventions were not assessed statistically) Of the 9 owners contacted 4 (1 SM, 3 S) had no improvement or deteriorated performance following surgery, 5 (3SM, 2 S) were reported to have improved but did not race for unrelated reasons
Adverse effects	Not reported
Main study limitations	Definitive diagnosis not achieved. Choice of intervention not randomised, baseline characteristics may vary between groups (sternothyrohyoideus myectomy was performed on significantly more TB and staphylectomy performed in significantly more SB) Less than 80% of horses that underwent surgery were included in the analysis. Adverse effects not reported 5% of horses had concurrent epiglottal entrapment

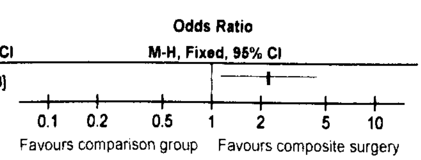
	which appears to be untreated, and therefore may affect success rate.

Study or Subgroup	Myectomy Events	Myectomy Total	Staphylectomy Events	Staphylectomy Total	Odds Ratio M-H, Fixed, 95% CI
Anderson et al 1995	48	80	41	69	1.02 [0.53, 1.98]



Barakzai *et al.* 2004	Journal publication
Study design	Cohort
Participants	104 TB racehorses underwent procedure, of which 53 (51%) were assessed. 106 TB racehorse comparison horses matched for age, sex and training yard.
Intervention assessed	Composite surgery (staphylectomy, sternothyrohyoideus myectomy and ventriculectomy)
Outcomes	Objective assessment determined by race earnings (3 races after intervention compared with 3 races before intervention).
Reported success of procedure	60% of treatment group had increased earnings compared with 41% of comparison population. There was a significant increase in earnings of surgical cases, there was no significant increase for the comparison group.
Adverse effects	Not reported
Main study limitations	Definitive diagnosis not achieved. Insufficient information to determine the validity of the comparison group. Less than 80% of horses that underwent surgery were included in the analysis. Adverse effects not reported

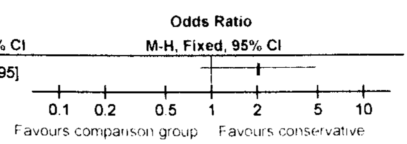
Study or Subgroup	Composite surgery Events	Composite surgery Total	Comparison group Events	Comparison group Total	Odds Ratio M-H, Fixed, 95% CI
Barakzai et al 2004	32	53	43	106	2.23 [1.14, 4.38]



Barakzai and Dixon 2005	Journal publication
Study design	Cohort
Participants	31 TB racehorses and 62 comparison horses matched for age and training yard.

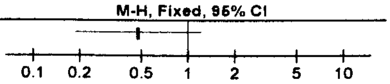
Interventions assessed	Conservative (rest, increased fitness, tongue tie) versus comparison group.
Outcomes	Objective assessment determined by race earnings (3 races after intervention compared with 3 races before intervention).
Reported success of procedure	Reported success rate of 61% for treatment group compared with 44% for comparison group. There was a significant increase in earnings for conservative cases, there was no significant increase for comparison horses.
Adverse effects	Not reported
Main study limitations	Definitive diagnosis in only 9 of 31 (29%) Insufficient information to determine the validity of the comparison group The number of trainers unwilling to participate in the study and the number of horses excluded from the study was not provided, creating a likely selection bias towards horses where conservative treatment was successful, as horses which had subsequent surgical treatment were excluded from the study. The conservative treatments are assessed as one group and it is unclear what proportion of horses were advised which treatment.

	Conservative treatment		Comparison group		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	M-H, Fixed, 95% CI
Barakzai and Dixon 2005	19	31	27	62	2.05 [0.85, 4.95]



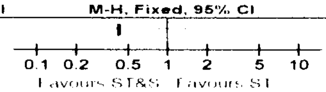
Barakzai *et al.* 2009a	Journal publication
Study design	Parallel group pre post
Participants	78 TB racehorses
Interventions assessed	Palatoplasty by thermal cautery (n=48) versus a combination of conservative interventions (drop noseband, tongue tie, rest or improve fitness) (n=30).
Outcomes	Objective assessment based on improvement in race earnings.
Reported success of procedure	3 races pre v 3 races post: 53% conservative and 35% cautery treated horses improved. 1 race pre v 3 races post: 63% conservative and 40% cautery treated horses improved 1 race pre v 5 races post: 60% conservative and 40% cautery treated horses improved. There was no statistically significant differences in the proportion of horses that improved in conservatively treated versus cautery groups.

	When the difference between earnings pre and post treatment was analysed as a continuous variable, using corrected data, there was no significant difference between conservative and cautery groups. No significant increase in earnings for either group when 3 races v 3 races, or 1 race v 5 races. When 1 race pre v 3 races post was assessed there was a significant increase in earnings for conservative group but not cautery group
Adverse effects	No intra or post operative complications were experienced in the cautery group
Main study limitations	Choice of intervention not randomised, some baseline characteristics vary between groups (although differences in baseline earnings were accounted for in one analysis). Unclear how many horses had an intervention and were not included in the analyses The conservative treatments were assessed as one group and it is unclear what proportion of horses were advised which treatment.

Study or Subgroup	Thermal cautery Events	Total	Conservative Events	Total	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Barakzai et al 2009	17	48	16	30	0.48 [0.19, 1.22]	

Bonenclark *et al.* 1999	Conference proceedings
Study design	Parallel group pre post
Participants	87 TB racehorses, of which 48 (55%) were included in analysis
Interventions assessed	Sternothyroideus tenectomy (ST) (n=30) versus sternothyroideus tenectomy with staphylectomy (ST&S) (n=18)
Outcomes	Objective assessment using improved race earnings (3 races after compared with 3 races before)
Reported success of procedure	60% improved following ST 78% improved following ST&S (Comparisons between interventions were not assessed statistically)
Adverse effects	Not reported
Main study limitations	Unknown how many had definitive diagnosis Choice of intervention not randomised, some baseline characteristics may vary between groups Less than 80% of horses that underwent surgery were

	included in the analysis. Adverse effects not reported

Study or Subgroup	ST Events	ST Total	ST&S Events	ST&S Total	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
BonenClark et al 1999	18	30	14	18	0.43 [0.11, 1.62]	

Cheetham *et al.* 2008	Journal publication
Study design	Cohort
Participants	263 horses underwent procedure of which 106 (68 TB, 38 SB) (40%) were included in analysis. Comparison horses matched for age, breed and sex from the 3rd race prior to surgery.
Interventions	Original technique in 32 cases; modified technique in 74 cases
Outcomes	Objective assessment using race earnings for up to 4 races pre and post operatively Presence of at least one post operative start
Reported success of procedure	Adjusted transformed earnings show that the procedure appears to restore earnings to baseline values and those of the comparison group. A more dorsal basihyoid and more dorsal and less rostral thyroid cartilage were associated with an increased probability of racing
Adverse effects	Not reported
Main study limitations	Definitive diagnosis of DDSP in 34% and palatal instability in 12%. Insufficient information to determine the validity of the comparison group. Less than 80% of horses that underwent surgery were included in the analysis (however exclusions were mostly because digital radiographs were not available, which may reduce the effect of this bias). Although the conclusions state that the surgery restores race earnings to preoperative baseline values, the study does not state in what proportion of horses this occurs. Variation in surgical technique, including addition of sternothyroid tenectomy (Ducharme 2005) Adverse effects not reported

Dart *et al.* 2006	Letter
Study design	Case report of adverse effects

Participant	One horse
Intervention assessed	Laryngeal tie-forward
Outcomes	Objective assessment using treadmill endoscopy pre and post intervention
Reported success of procedure / Adverse effects	Initial endoscopy revealed DDSP and no vocal fold collapse. Endoscopy post laryngeal tie-forward revealed DDSP persisted and the horse had developed bilateral vocal fold collapse
Main study limitations	Single case report The horse was rested for three months prior to the laryngeal tie-forward procedure being performed. It may have been possible for the vocal fold collapse to have occurred during this time frame rather than as a result of surgery.

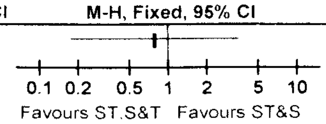
Duncan 1997	Conference proceedings
Study design	Pre post
Participants	50 TB racehorses.
Intervention assessed	Sternothyroideus, sternohyoideus and omohyoideus myectomy
Outcomes	Objective assessment using average race earnings per start before and after intervention.
Reported success of procedure	70% had increased earnings per start
Adverse effects	Minor haemorrhage and seroma formation
Main study limitations	Definitive diagnosis not achieved No comparison group The mean and median number of starts was considerably higher after surgery than before; this may affect the apparent success rate because horses have more chances to earn stakes (and increase in class) after surgery. Insufficient details regarding adverse effects

Dykgraaf *et al.* 2005	Conference proceedings
Study design	Parallel group pre post
Participants	96 TB racehorses, of which 77 (80%) were included in analysis by the authors. Of these 13 horses were excluded from this review as it was not possible to determine which had sternothyroideus tenectomy alone and which had sternothyroideus tenectomy in conjunction with thermoplasty and 6 were excluded

	because of concurrent surgery for epiglottic entrapment.
Interventions assessed	Sternothyroideus tenectomy and staphylectomy (ST&S) (n=49), or sternothyroideus tenectomy, staphylectomy and thermoplasty (ST,S&T) (n=9).
Outcomes	Objective assessment using total race earnings for up to 3 races before and after intervention
Reported success of procedure	61% ST&S improved 67% ST,S&T improved (Comparisons between interventions were not assessed statistically)
Adverse effects	Not reported
Main study limitations	Unclear how many had a definitive diagnosis Choice of intervention not randomised, baseline characteristics may vary between groups. Some groups have small sample size Adverse effects not reported

Study or Subgroup	ST&S Events	ST&S Total	ST.S&T Events	ST.S&T Total	Odds Ratio M-H, Fixed, 95% CI
Dykgraaf et al 2005	30	49	6	9	0.79 [0.18, 3.54]

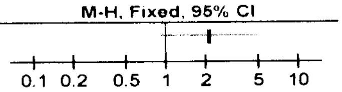
Odds Ratio
M-H, Fixed, 95% CI

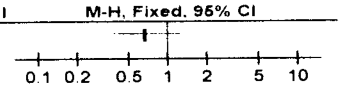


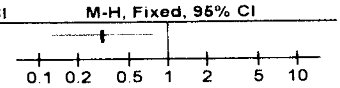
Franklin *et al.* 2002	Journal publication
Study design	Pre post
Participants	6 TB racehorses
Intervention assessed	Tongue tie (TT)
Outcomes	Objective assessment using treadmill endoscopy, run-time to fatigue, time at which DDSP occurred and measurement of respiratory parameters.
Reported success of procedure	All horses had DDSP without a TT. 4 horses still experienced DDSP with a TT. In 2 horses (33%) palatal instability and not DDSP was observed with a TT. 3 horses had DDSP earlier in the test with a TT compared to without TT, however this was not statistically significant The TT did not result in any significant alteration in run-time to fatigue or in any of the respiratory variables measured.
Adverse effects	Not reported

Main study limitations	Small sample size No comparison group As no repeatability studies for DDSP have been undertaken, it is unclear whether palatal instability should be considered a success.

Franklin *et al.* 2009	Conference proceedings, oral presentation and unpublished data
Study design	Parallel group pre post
Participants	234 TB racehorses, of which 197 (84%) included in analysis
Interventions assessed	Palatoplasty by thermal cautery (SPC) (n= 103), laryngeal tie-forward (LTF) (n=31), laryngeal tie-forward and thermal cautery combined (LTF+SPC) (n=63).
Outcomes	Objective assessment based on improvement in race earnings and racing post ratings for 1v1, 2v2, 3v3, 4v4 and 1v3 races before and after intervention.
Reported success of procedure	Success rates varied depending on which measure of race performance was used. 32-59% for SPC 26-62% for LTF 38-73% for LTF+SPC No significant difference in success rate between interventions for 4 races before and after surgery. However there was a significant difference in earnings between groups for 3 races before and after surgery, where success of LTF+SPC was significantly better than LTF alone. For the LTF there was no significant effect of implant material, of drilling the basihyoid or of additional sternothyroid tenectomy. For the SPC there was no significant effect of sub-epiglottic resection.
Adverse effects	Not reported
Main study limitations	Choice of intervention not randomised, baseline characteristics may vary between groups. Multiple statistical analyses were undertaken. Variation in surgical technique for both SPC and LTF. Adverse effects not reported

Study or Subgroup	SPC Events	SPC Total	LTF Events	LTF Total	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Franklin et al 2009	52	103	10	31	2.14 [0.92, 4.99]	

Study or Subgroup	SPC Events	SPC Total	LTF+SPC Events	LTF+SPC Total	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Franklin et al 2009	52	103	38	63	0.67 [0.36, 1.27]	

Study or Subgroup	LTF Events	LTF Total	LTF+SPC Events	LTF+SPC Total	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Franklin et al 2009	10	31	38	63	0.31 [0.13, 0.78]	

Llewellyn and Petrowitz 1997	Conference proceedings
Study design	Pre post
Participants	405 SB racehorses, of which 41 (10%) were randomly selected for analysis
Intervention assessed	Sternothyroideus myotomy and staphylectomy
Outcomes	Objective assessment using adjusted racetimes, in one season
Reported success of procedure	71% horses showed some improvement in race times
Adverse effects	Haemorrhage, exuberant palatine granulation tissue, postoperative swelling and redevelopment of DDSP
Main study limitations	Definitive diagnosis not achieved No comparison group Less than 80% of horses that underwent surgery were included in the analysis, however random selection may reduce the effect of this bias. Unclear how many races before and after the intervention was assessed. Insufficient details on numbers of horses experiencing adverse effects

Marcoux *et al.* 2008	Journal publication
Study design	Pre post
Participants	8 SB
Intervention assessed	Palatal sclerotherapy using 3% sodium tetradecyl sulphate.

Outcomes	Subjective assessment of performance by trainer or referring veterinarian of side effects, respiratory noise and performance.
Reported success of procedure	Some improvement in abnormal noise in 7 horses. All horses unraced before, 6 able to race after procedure. 7 of 8 horses require second treatment.
Adverse effects	1 horse had temporary mucosal bleeding, 2 slight coughing of which 1 had pyrexia. 1 horse had lump (<2mm) at one injection site.
Main study limitations	Definitive diagnosis not achieved No comparison group Small sample size Outcome measure subjective. Unclear how accurate a percentage improvement in noise is.

McCluskie *et al.* 2009	Conference proceedings and oral presentation
Study design	Parallel group pre post study (multiple groups)
Participants	116 horses diagnosed with palatal dysfunction and were offered repeat treadmill endoscopic examination, of which 37 horses (32%) (35 TB racehorses, 1SB, 1 eventer) were assessed by the authors. A total of 42 interventions were assessed of which 29 interventions for palatal dysfunction alone are reported here.
Interventions assessed	Palatoplasty by thermal cautery (SPC) (n=12), laryngeal tie-forward (LTF) (n=8), laryngeal tie-forward in combination with thermal cautery (SPC+LTF) (n=9).
Outcomes	Objective assessment based upon treadmill endoscopic examination before and after intervention. Subjective assessment by trainer. Run time to fatigue assessed pre and post intervention
Reported success of procedure	Of horses diagnosed with DDSP (n=21): 3/6 SPC still had DDSP 7/8 LTF still had DDSP 3/7 SPC+LTF still had DDSP When DDSP did not occur, all horses were observed to have palatal instability, no horse was observed to have normal palate function post surgery. Of horses initially diagnosed with palatal instability (PI) (n=8): 5/6 SPC still had PI (1 had DDSP) 2/2 LTF+SPC still had PI. No significant difference between surgery type and improvement in soft palate function

	Significant decrease in run time to fatigue post intervention compared with pre intervention. There was no correlation between trainer assessment of improvement and endoscopic improvement.
Adverse effects	Not reported
Main study limitations	Choice of intervention not randomised, baseline characteristics may vary between groups. Less than 80% of horses that underwent surgery were reassessed. Potential bias whereby horses still poorly performing or making abnormal noise may be more likely to return for repeat treadmill examination than horses performing well. Small sample size Unclear whether DDSP pre intervention and PI post intervention should be considered success, particularly as horses had reduction in run-time in the second test. Variation in surgical technique for both SPC and LTF. In 5 horses more than one intervention was performed. Adverse effects not reported

Ordidge 2001	Conference proceedings
Study design	Pre post
Participants	252 TB racehorses, of which 187 (74%) were assessed
Intervention assessed	Palatoplasty by thermal cautery
Outcomes	Subjective assessment by trainer of abnormal noise and race performance
Reported success of procedure	72% of horses were considered to be successfully treated 82/171 (48%) of horses ceased making a 'gurgling' noise
Adverse effects	Not clearly described – discomfort up to 36 hours
Main study limitations	No definitive diagnosis achieved No comparison group Less than 80% of horses that underwent surgery were included in the analysis. Subjective assessment only Insufficient details regarding adverse effects

Parente *et al.* 2002	Journal publication
Study design	Parallel group pre post
Participants	92 racehorses (74 TB, 18 SB), of which 32 (35%) were assessed.
Interventions assessed	Sternothyroid tenectomy and staphylectomy (n=11),

	sternothyroid myectomy (n=7), epiglottic augmentation (n=8) or conservative treatment (n=6).
Outcomes	Objective assessment using average earnings per start for three races before and after treatment
Reported success of procedure	73% improved with sternothyroid tenectomy and staphylectomy 50% improved with sternothyrohyoid myectomy 50% improved with epiglottic augmentation 100% improved with conservative treatment (oral steroids and rest) (Comparisons between interventions were not assessed statistically)
Adverse effects	Not reported
Main study limitations	Choice of intervention not randomised, baseline characteristics may vary between groups Small sample size Less than 80% of horses that underwent surgery were included in the analysis. 35 horses had additional upper respiratory tract obstructions and it is unclear which horses with complex obstructions had which treatment. It is unclear whether these were addressed and hence may have an impact on success rates. Adverse effects not reported

Forest plot not created due to difficulty extracting appropriate data -the myectomy group was reported to contain 7 horses of which 50% improved.

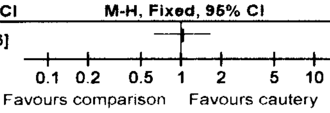
Peloso *et al.* 1992	Journal publication
Study design	Case report
Participants	One SB
Intervention assessed	Sternothyrohyoideus myectomy Epiglottic augmentation using polytetrafluoroethylene
Outcomes	Objective assessment using treadmill endoscopy on 3 occasions pre and post intervention
Reported success of procedure	DDSP observed on all 3 occasions pre intervention. DDSP observed on all 3 occasions post sternothyrohyoideus myectomy and was considered ineffective. DDSP was not observed on any occasion post epiglottic augmentation and was considered successful
Adverse effects	Epiglottic augmentation - endoscopy revealed epiglottic oedema, reddening, and persistent DDSP. Oedema and discolouration decreased over 23 days.

	Horse coughed for 3 weeks post surgery.
Main study limitations	Single case report No information provided that the horse performed the same treadmill speeds and distance as prior to surgery.

Picandet *et al.* 2005	Conference proceedings
Study design	Pre post
Participants	51 SB
Intervention assessed	Palatal sclerotherapy using 3% sodium tetradecyl sulphate.
Outcomes	Subjective assessment of improved performance and abnormal noise Objective assessment of race times for two races before and after intervention
Reported success of procedure	70% of horses reported to improve race times by >50% 60% of horses making respiratory noise ceased to do so Post treatment horses significantly reduced their time in the last part of the race compared with pre treatment.
Adverse effects	Slight side effects (details unspecified)
Main study limitations	Definitive diagnosis not achieved No comparison group Insufficient details regarding adverse effects

Reardon *et al.* 2008a	Journal publication
Study design	Cohort
Participants	110 TB racehorses; 220 comparison TB racehorses matched for age, sex and training yard.
Intervention assessed	Palatoplasty by thermal cautery
Outcomes	Objective assessment based upon ratings, earnings and performance index for up to 3 races pre and post intervention
Reported success of procedure	3 races pre v 3 races post Earnings: 34% of cautery group improve, 33% of comparison group improve Ratings: 51% of cautery group improve, 53% of comparison group improve Performance index: 28% of cautery group improve, 21% of comparison group improve Cases had a significant decrease in earnings, ratings and performance index compared with comparison horses in the last race before surgery.

	There was no significant effect of cautery on the change in ratings or earnings between cautery and comparison groups for 3 races pre and post. Although there was a significant effect on performance index, this was thought to be clinically insignificant because of the large percentage of horses that showed no change.
Adverse effects	No reported complications following the procedure
Main study limitations	Definitive diagnosis not achieved. Insufficient information to determine the validity of the comparison group. Unclear how many horses had an intervention and were not included in the analyses

Study or Subgroup	Cautery Events	Cautery Total	Comparison Events	Comparison Total	Odds Ratio M-H, Fixed, 95% CI	Odds Ratio M-H, Fixed, 95% CI
Reardon et al 2008	37	110	73	220	1.02 [0.63, 1.66]	

Reardon *et al.* 2008b	Conference proceedings and oral presentation
Study design	Cohort
Participants	98 TB racehorses, of which 43 (44%) were assessed and 24 of these were matched with a comparison horse.
Intervention assessed	Laryngeal tie-forward in combination with palatoplasty by thermal cautery
Outcomes	Objective assessment based upon race ratings, earnings and performance index for up to 3 races pre and post intervention
Reported success of procedure	For the 43 horses (3 races pre v 3 races post) 67% improved earnings (RE) 44% improved performance index (Perf. I) 63% improved racing post rating (RPR) 55% improved timeform rating 42% improved official rating There was a significant improvement in RE, Perf. I and RPR in the first race post surgery compared with the last race pre surgery. For the 24 horses: Cases had a significant difference in RE, Perf. I and RPR compared with comparison horses in the last race before surgery, but not after surgery. A comparison of 3 races pre and post found no significant difference between cases and comparison horses.

Adverse effects	Not reported
Main study limitations	Definitive diagnosis not achieved. Insufficient information to determine validity of comparison group Less than 80% of horses that underwent surgery were included in the analysis. Adverse effects not reported

Smith and Embertson 2005	Journal publication
Study design	Pre post
Participants	102 TB racehorses, of which 73 (72%) were assessed
Intervention assessed	Sternothyroideus myotomy, staphylectomy and oral caudal soft palate photothermoplasty
Outcomes	Objective assessment using earnings per start for up to 3 races before and after surgery
Reported success of procedure	63% of horses significantly improve earnings per start post intervention compared with pre intervention
Adverse effects	No complications were reported in any horse
Main study limitations	Unclear how many had definitive diagnosis No comparison group Less than 80% of horses that underwent surgery were included in the analysis

Woodie *et al.* 2005a	Journal publication
Study design	Pre post
Participants	116 horses (61 SB, 54 TB, 1 WB), of which 98 (84%) assessed by trainer and 61 (53%) included in race performance analysis. Some horses (group 5) had additional surgery and were excluded from this review. Only the results of 20 horses (group 1) were reported separately by the authors and therefore could be included in this review.
Intervention assessed	Laryngeal tie-forward, original technique
Outcomes	Objective assessment using performance index and sum of pre and post earnings calculated for 3 races pre and post intervention Repeat treadmill endoscopy (n=3) (Subjective analysis by trainer included in analysis in original study but could not be included in this review)
Reported success of procedure	80% had improved earnings and performance index. Pre operative PI and race earnings were significantly

	lower than post operative PI and race earnings. 3 horses reassessed by repeat treadmill endoscopy, in 1 horse DDSP was observed, in 2 no DDSP was observed.
Adverse effects	8 of the 116 (7%) experienced complications (difficulty swallowing (n=1), incisional swelling/seroma (n=4), upper airway dyspnoea (n=1), laryngeal granuloma (n=1), difficulty eating off floor (n=1). 6% of 85 horses in the improved category reported to have recurrence of DDSP.
Main study limitations	No comparison group Less than 80% of horses that underwent surgery were assessed objectively.

Appendix III: Excluded studies

Study Reference	Reason for exclusion
Ahern, T. (1993) Oral palatopharyngoplasty. *J. equine vet. Sci.* **13**, 185-188.	Criteria for successful outcome undefined.
Barakzai, S. and Dixon, P.M. (2004) Conservative treatment for thoroughbred racehorses affected with dorsal displacement of the soft palate. *Proc. Br. equine vet. Assoc. Congress.* p 98.	Same data as Barakzai and Dixon (2005) which is included in review.
Barakzai, S. (2007) Conservative management of dorsal displacement of the soft palate. *Proc. Br. equine vet. Assoc. Congress.* p 345.	No original trial data.
Barakzai, S.Z., Finnegan, C. and Boden, L.A. (2009b) Effect of tongue tie use on racing performance of Thoroughbreds in the United Kingdom. *Equine vet. J.*, **41**, 812-816.	DDSP was not diagnosed by the authors
Barber, S., Fretz, P.B., Bailey, J. and McKenzie, N. (1984) Analysis of surgical treatments for selected upper respiratory tract conditions in horses. *Veterinary Medicine and small animal clinician* **79**, 678-682.	Case history does not describe intermittent DDSP during exercise
Baudler, A., Luetkefels, E., Drommer, W., Deegan, E and Ohnesorge B. (2003) Experimental studies on epiglottic hypoplasia in horses: transendoscopic injection of collagen and polytetrafluoroethylene. *Dtsch Tieraerztl Wschr* **110**, 160-165.	Experimental study in normal horses Article in German
Beard, W.L., Holcombe, S.J. and Hinchcliff, K.W. (2001) Effect of a tongue-tie on upper airway mechanics during exercise following sternothyrohyoid myectomy in clinically normal horses. *Am. J. vet. Res.* **62**, 779-782.	Experimental study in normal horses
Beard, W.L. and Waxman, S. (2007) Evidence-based equine upper respiratory surgery. *Vet. Clin. N. Am.: Equine Pract.* **23**, 229-242.	Review
Bertuglia, A. (2006) Standing surgery for sternothyroideus myotomy and caudal soft palate thermoplasty. *Proc. 12th SIVE Congress* (www.ivis.org)	Abstract in Italian
Boles, C. (1979) Treatment of upper airway abnormalities. *Vet. Clin. N. Am.: Large Animal Pract.* **1**, 127-147.	No pre post data
Carter, B.G., Robertson, J.T., Beard, W.L. and Moore, R.M. (1993) Sternothyrohyoideus myectomy, tenectomy and staphylectomy for the treatment of dorsal displacement of the soft palate in horses. (ACVS abstract) *Vet. Surg.* **22**, 374.	No pre post data published in abstract

Cehak, A., Deegan, E., Drommer, W., Lutkefels, E. and Ohnesorge, B. (2006) Transendoscopic injection of poly-L-lactic acid into the soft palate in horses: a new therapy for dorsal displacement of the soft palate? *J. equine vet. Sci.* **26**, 59-66.	Experimental study in normal horses
Cheetham, J., Pigott, J., Mohammed, H. and Ducharme, N. (2008) Outcome based assessment of the laryngeal tie-forward procedure and its effect on hyoid conformation. *Proc. Am. College vet. Surg. Congress.* p 7	Same data as Cheetham *et al.* (2008) Racing performance following the laryngeal tie-forward procedure: A case-controlled study. *Equine vet. J.* 40, 501-507 which is included in review.
Cook W.R. (1962) Clinical observations on the equine soft palate. *British Equine Veterinary Association Bulletin.* 1, 5-9.	Published prior to 1990
Cook, W. R. (2002) Bit-induced asphyxia in the horse: elevation and dorsal displacement of the soft palate at exercise. *J. equine vet. Sci.* **22**, 7-14.	No trial data
Cook, W.R. (2005) Treatment for dorsal displacement of the soft palate in horses. *Vet. Rec.* **157**, 752.	No trial data
Cook, W.R. and Chandler, N. (1978) Sternothyrohyoid myectomy in the treatment of soft palate problems. *Proc. Br. equine vet. Assoc. Congress.* p 40	Published prior to 1990
Cornelisse, C.J., Holcombe, S.J., Derksen, F.J., Berney, C. and Jackson, C.A. (2001) Effect of a tongue-tie on upper airway mechanics in horses during exercise. *Am. J. vet. Res.* **62**, 775-778.	Experimental study in normal horses
Delfs, K.C., Hawkins, J.F., Lescun, T.B., Widmer, W.R., Miller, M.A. and Couetil, L. (2008) Soft palate laser palatoplasty in the horse using the diode laser: a clinical, histopathological, MRI and biomedichanical examination. *Proc. Am. College vet. Surg. Congress.* p 9	Experimental study in normal horses
Ducharme, N.G. (2008) Update on management of DDSP. *Proc. 14th SIVE/FEEVA Congress.* 113-115.	No original trial data
Ducharme, N.G. (2003) Management options for DDSP. *Proc. Br. equine vet. Assoc. Congress*, 134-135.	No trial data
Ducharme N.G. (2005) Management of DDSP: Tie Forward and Throat Support Devices. *Proc. 3rd World Equine Airways Symposium.* 107-108.	No original trial data
Ducharme, N.G. (2008) Update on laryngeal tie-forward operation. *Proc. 14th SIVE/FEEVA Congress.* 99-101.	Insufficient details on how outcome was assessed
Dugdale, D. and Greenwood, R. (1993) Some observations on conservative techniques for treatment of laryngopalatal displacement. *Equine Vet. Educ.* **5**,	No pre post trial data

177-180.	
Duggan, V.E., MacAllister, C.G. and Davis, M.S. (2002) Xylazine-induced attenuation of dorsal displacement of the soft palate associated with epiglottic dysfunction in a horse. *J. Am. Vet. Med. Assoc.* **221**, 399-401.	Case report is persistent DDSP, and describes clinical observations following administration of xylazine. Xylazine could not reasonably be used as a treatment for DDSP.
Dykgraaf, S., McIlwraith, C.W., Baker, V.A., Byrd, W.J. and Daniel, R.C. (2008) Sternothyroideus tenectomy combination surgery: treatment outcome in 95 thoroughbred racehorses (1996-2006). *J. equine vet. Sci.* **28**, 598-602.	Same horses as Dykgraaf *et al.* (2005) which are included in the review. The results of each combination of surgeries were only presented in Dykgraaf *et al.* (2005) not in this paper.
Franklin, S.H., McLachlan, C.E. and Lane, J.G. (2001) The treatment of dorsal displacement of the soft palate in Thoroughbred horses in training. *Proc. Br. Equine Vet. Assoc. Congress.* 211.	Survey of trainers opinions
Gerstenberg, C. and Dugdale, D. (1998) Transendoscopic Nd:YAG laser surgery to treat dorsal displacement of the soft palate. *Proc. Br. equine vet. Assoc. Congress.* p 111-112.	Insufficient details on outcome following procedure.
Hackett, R.P., Ducharme, N.G. and Rehder, R.S. (1992) Use of the high speed treadmill in management of horses with dorsal displacement of the soft palate. *Proc. Am. Ass. Equine Practnrs.* **38**, 153.	Unclear which outcome relates to which intervention
Harrison, I.W. and Raker, C.W. (1988) Sternothyrohyoideus myectomy in horses: 17 cases (1984-1985). *J. Am. Vet. Med. Assoc.* **193**, 1299-1302.	Published prior to 1990
Haynes, P.F. (1983) Dorsal displacement of the soft palate and epiglottic entrapment: diagnosis, management and interrelationship. *Comp. Cont. Educ.* 5, 379-389.	No trial data
Hogan, P., Palmer, S. and Congelosi (2002) Transendoscopic laser cauterisation of the soft palate as adjunctive treatment for dorsal displacement of the soft palate in racehorses. *Proc. Am. Ass. Equine Practnrs.* **48**, 228-230.	Some horses had additional sternothyroideus tenectomy. Unclear which outcome relates to which intervention.
Holcombe, S.J., Beard, W.L., Hinchcliff, K.W. and Robertson, J.T. (1994) Effect of sternothyrohyoid myectomy on upper airway mechanics in normal horses. *J. Appl. Physiol.* **77**, 2812-2816.	Experimental study in normal horses
Holcombe, S.J. (2007) Surgical management of intermittent dorsal displacement of the soft palate. *Proc. Br. equine vet. Assoc. Congress* p347.	No original trial data.
Honnas, C.M. (1990) Identifying and correcting displacement of the soft palate and pharyngeal tissues. *Vet. Med.* **85**, 622-631.	No original trial data

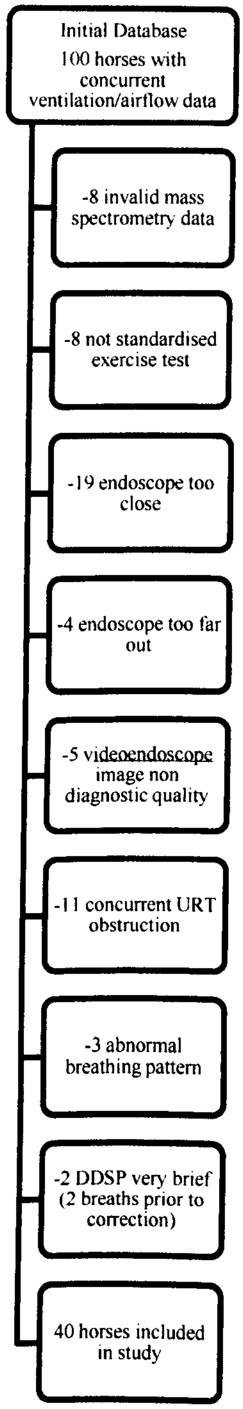
Jager-Hauer, K., Lutkefels, E., Deegan, E., Drommer, W. and Ohnesorge, B. (2003) Experimental study on transendoscopic laser surgery of dorsal displacement of the soft palate in horses. *Tierarztl Prax Ausg G Grosstiere Nutztiere* **31**, 18-24.	Experimental study in normal horses
Jansson, N. (2006) Dorsal displacement of the soft palate in horses - new methods of treatment. *Danske Veterinaertidsskrift* **89**, 10-11.	No original trial data in abstract
Koch, C. (1991) Augmentation of the equine epiglottis with Teflon paste. *Proc. Am. Ass. Equine Practnrs.* **36**, 541-545.	Some horses had concurrent staphylectomy, unclear which outcome relates to which intervention
Lane, J.G. (1993) DDSP, epiglottic entrapment and related conditions. *Proceedings of 15th Bain Fallon Memorial Lectures, Australian Equine Veterinary Association*, 193-206.	No original trial data
Lane, J.G. (2001) Surgery for DDSP: how can it be rationalised? *Proc. Br. equine vet. Assoc. Congress*, 90-91.	No original trial data
Ohnesorge, B. and Deegen, E. (1998) [Transendoscopic laser surgery of exercise-induced dorsal displacement of the soft palate in horses]. *Tierarztl Prax Ausg G Grosstiere Nutztiere* **26**, 287-293.	Article in German
O'Rielly, J.L., Beard, W.L., Renn, T.N., Padden, A.J. and Hinchcliff, K.W. (1997) Effect of combined staphylectomy and laryngotomy on upper airway mechanics in clinically normal horses. *Am. J. vet. Res.* **58**, 1018-1021.	Experimental study in normal horses
Reardon, R.J.M., Bladon, B.M., and Lane, J.G. (2007) Oral palatopharyngoplasty for treatment of horses with signs associated with intermittent dorsal displacement of the soft palate. A case control study in 78 racing thoroughbreds. *Proc. Br. equine vet. Assoc. Congress.* p 298-299.	Proportion of horses underwent concurrent tenectomy, but results assessed as one group.
Robertson, J.T. and Copelan, R.W. (1990) Surgery of the upper respiratory tract in the racehorse. *Vet. Clin. N. Am.: Equine Pract.* **6**, 197-222.	No pre post trial data
Stehle, C., Rocken, M., Mosel, G., Rass, J. and Litzke, L. (2006) Transendoscopic laser-surgery of the dorsal displacement of the soft palate in horses: surgical technique, rate of success, prognosis. *Tierarztl Prax Ausg G Grosstiere Nutztiere* **34**, 110-115.	Article in German
Tate, L.P., Sweeney, C.L., Bowman, K.F., Newman, H.C. and Duckett, W.M. (1990) Transendoscopic Nd:YAG laser surgery for treatment of epiglottal entrapment and dorsal displacement of the soft palate in the horse. *Vet. Surg.* **19**, 356-363.	DDSP was either persistent or associated with epiglottic entrapment

Toth, F. and Cole, R. (2006) Epiglottic augmentation surgery for the treatment of intermittent dorsal displacement of the soft palate in the horse. *Magyar Allatorvosok Lapja* **128,** 323-327.	No pre post trial data in abstract
Tulleners, E., Mann, P. and Raker, C.W. (1990) Epiglottic augmentation in the horse. *Vet. Surg.* **19**, 181-190.	Experimental study in normal horses
Tulleners, E. and Hamir, A. (1991) Evaluation of epiglottic augmentation by use of polytetrafluoroethylene paste in horses. *Am. J. vet. Res.* **52,** 1908-1915.	Experimental study in normal horses
Tulleners, E., Stick, J.A., Leitch, M., Trumble, T.N. and Wilkerson, J.P. (1997) Epiglottic augmentation for treatment of dorsal displacement of the soft palate in racehorses: 59 cases (1985-1994). *J. Am. vet. med. Assoc.* **211**, 1022-1028.	Different combinations of surgery were performed, but results were analysed as one group
Wiley, M. (1993) Electrosurgical approach to correction of dorsal displacement of the soft palate. *J. equine vet. Sci.* **13**, 4-6.	No pre post data specified
Woodie, J.B., Ducharme, N.G., Hackett, R.P., Erb, H.N., Mitchell, L.M. and Soderholm, L.V. (2005) Can an external device prevent dorsal displacement of the soft palate during strenuous exercise? *Equine Vet. J.* **37**, 425-429.	Experimentally induced DDSP
Zertuche, J., Turner, T. and Colahan, P. (1990) Strap muscle myectomy for treatment of idiopathic intermittent dorsal displacement of the soft palate in the racing Thoroughbred. (ACVS abstract) *Vet. Surg.* **19**, 82.	Insufficient data on how outcome was assessed in abstract

Appendix IV: The effect of palatal dysfunction on measures of ventilation and gas exchange in thoroughbred racehorses during high-intensity exercise.

Flow chart showing exclusions

Key: DDSP- dorsal displacement of the soft palate, URT- upper respiratory tract


Initial Database
100 horses with concurrent ventilation/airflow data
-8 invalid mass spectrometry data
-8 not standardised exercise test
-19 endoscope too close
-4 endoscope too far out
-5 videoendoscope image non diagnostic quality
-11 concurrent URT obstruction
-3 abnormal breathing pattern
-2 DDSP very brief (2 breaths prior to correction)
40 horses included in study

Publications

Journal articles:

Allen K.J., Christley R.M., Birchall M.A. and Franklin S.H. (2011) A systematic review of the efficacy of interventions for dynamic intermittent dorsal displacement of the soft palate. *Equine vet. J.* epub ahead of print.

Allen K.J., Hillyer M.H., Terron-Canedo N. and Franklin S.H. (2011) Equitation and exercise factors affecting dynamic upper respiratory tract function: a review illustrated by case reports. *Equine vet. Educ.* 23, 361-368.

Allen K.J. and Franklin S.H. (2010) Assessment of the exercise tests used during overground endoscopy in UK thoroughbred racehorses and how these may affect the diagnosis of dynamic upper respiratory tract obstructions. *Equine vet. J. suppl.,* 38, 587-591.

Allen K.J. and Franklin S.H. (2010) Comparisons of overground endoscopy and treadmill endoscopy in U.K. Thoroughbred racehorses. *Equine vet. J.* 42, 186-191.

Franklin S.H., Burn J.F. and **Allen K.J.** (2008) Clinical trials using a telemetric endoscope for use during over-ground exercise: A preliminary study. *Equine vet. J.* 40, 712-715.

Presentations:

Allen K.J. and Franklin S.H. (2010) Assessment of the exercise tests used during overground endoscopy in UK thoroughbred racehorses and how these may affect the diagnosis of dynamic upper respiratory tract obstructions. *International conference on equine exercise physiology*

Allen K.J. and Franklin S.H. (2009) Comparisons of overground endoscopy and treadmill endoscopy in UK thoroughbred racehorses. *World equine airways symposium.*

Allen K.J. (2009) Systematic review of interventions for DDSP. *Association of racecourse veterinary surgeons summer scientific meeting*